Transplantation Through the Generations

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Abstract

Whilst the basic principles of HSCT remain the same, regardless of the age of the patient, there are a number of important additional considerations relating to transplantation of our younger and older patients and those of adolescent age. The principles outlined in this chapter serve as a valuable reminder supporting age-appropriate patient-centred care delivery. This chapter initially focuses on transplanting the child and its physiological and psycho-social aspects. Subsequently, the nursing challenges in the AYA population will be addressed. This chapter ends with considerations for treatment and care for the older adult.

Keywords

HSCT · Paediatric · AYA · TYA · Older patients · Fragile · Geriatric problems · Geriatric assessment · Patient information · Decision making

9.1 Transplanting the Child

HSCT offers the ability to cure pediatric patients with blood cell diseases. In Europe, around 5000 children are transplanted on an annual basis. Different stages of growth and development can be identified during childhood. Undergoing HSCT has a major impact on children, their parents and siblings, especially when they have a double role

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M. Kenyon, A. Babic (eds.), *The European Blood and Marrow Transplantation Textbook for Nurses*,
https://doi.org/10.1007/978-3-031-23394-4_9

as family member and family donor. The ability to cure children with acquired or inherited disorders of the hematopoietic system has radically improved over the recent decades. Today, more than 80% of children with cancer are cured of their disease (Gatta et al. 2014). This incredible achievement is one of the greatest triumphs in the history of medicine and is the result of numerous factors, including developments in paediatric haematopoietic stem cell transplantation (HSCT). Treatment advances for the sick child have been accomplished in various treatments, including chemotherapy, surgery, radiotherapy, HSCT and CAR T-cell therapy. While these therapies have vastly improved outcomes in childhood diseases, there remains scope for further improvement.

9.1.1 The Role of EBMT in Paediatric HSCT

Changes in HSCT approaches are responsible for progress in this particular area. The role and status of transplantation have evolved. It is no longer considered a salvage therapy for patients in desperate circumstances but is now the treatment of choice for many diseases. The history of paediatric HSCT in Europe began in Poland in 1949 (Raszek-Rosenbusch), with therapeutic transfusion of bone marrow in children with leukaemia and other blood diseases. Subsequent developments in paediatric HSCT were driven on by the creation in 1974 of the European Society for Blood and Marrow Transplantation (EBMT). The goal of the society remains to promote all aspects associated with HSCT. Since the launch of the EBMT Society in 1974, several working parties were established, and in 1995, the Board of the EBMT founded the Paediatric Diseases Working Party (PDWP). Shortly after, the registry of the EBMT began to analyse transplant outcomes in children and adolescents, increasing our understanding, which in turn informed changes and developments in the field. The continuous progressions and evolution of paediatric HSCT in Europe have resulted in the establishment of HSCT as a standard therapeutic procedure in paediatric haemato-oncology and immunology.

The number of children and adolescents undergoing HCST has been steadily increasing since the 1980s. It is clear that close national and international collaboration between HSCT units helps resolve common difficulties with this complex treatment. The scale of collaboration within the EBMT members is underpinned by EBMT's annual transplant activity surveys.

Over the last 30 years, more than 800,000 HSCTs in 715,000 patients have been reported (Passweg et al. 2021). Between 2016 and 2020, the annual amount of paediatric HSCTs varied between 4690 and 5368, of which around 25% were autologous (Passweg et al. 2018, 2019, 2020, 2021, 2022).

Main indications for pediatric HSCTs are myeloid and lymphoid malignancies and non-malignant disorders (Passweg et al. 2021, 2022). The high proportion of allogeneic transplants in paediatrics is largely due to the characteristics of paediatric diseases that are amenable to transplantation such as haemoglobinopathies, immune deficiencies, immune dysregulation and metabolic diseases.

9.1.2 Child Growth and Development

It is important to know and understand the developmental stages of infants and children because appreciation of the ages, stages, common milestones and abilities allows nurses to relate to the children and their relatives appropriately. The knowledge of the normal growth and development equips the nurses to identify any developmental delay. Growth and development are a single process, which begins during pregnancy and continues throughout childhood and into adolescence. Growth is a change in the body size and structure, whilst development is a change in the body function.

Child growth refers to progressive structural and physiological changes in the size of a child body. Physical growth includes gaining full height and appropriate weight and increasing in size of all organs. The measurements of weight, length, head circumference, body composition

and tooth eruption aid in assessment of normal and standard physical growth (Mona 2015).

Child development concerns a child's ability to undertake more complex processes as they mature. Child development is subdivided into specific areas, such as motor, language, cognitive, behavioural and emotional.

9.1.3 The Child and the Experience of Disease

The child is aware of the condition and often the severity of their disease whatever his age (Badon and Cesaro 2015). This consciousness derives primarily from their perception of the body and wellness state changes. Furthermore, a child's disease awareness is determined by the child's own level of cognitive function, previous experiences, psycho-emotional structure and the quality of relationships established with reference figures. These factors impact upon a child's ability to understand the meaning and significance of what is happening and how they respond on it.

9.1.3.1 Hospitalisation

The child is sensitive to the experience of disconnection that disease imposes. The disease acts as a breaking event in the life of the child and alters the way the body is considered and treated. Hospitalisation changes the physical and relational environment and modifies the emotional climate and the usual style of education.

During hospitalisation, the child's world is changed; for instance, they are relieved of responsibilities, and many rules disappear or are replaced. They become the target of therapeutic measures, sometimes with little consideration for privacy or confidentiality, and the child becomes separated from their own world. If this disconnect remains within the child's limits of tolerance, it is absorbed into their normal development. However, if this disconnect exceeds their tolerance, it results in a traumatic experience and becomes in itself a source of anxiety and distress (Badon and Cesaro 2015).

The child often does not have the ability to understand the causes and the logic of the events that lead suddenly to being excluded from their family environment, separated from significant figures and entrusted to the care of strangers. The child will tend to experience hospitalisation with a sense of danger that derives primarily from the inability to understand and control the absent parent (Badon and Cesaro 2015).

9.1.4 The HSCT Experience

HSCT is usually an elective, planned treatment. Children who suffer from malignant disease and undergo transplantation often have experienced previous treatments and hospitalisations for treatment of complications such as fever, pain, mucositis, nausea and vomiting as well as periods of isolation. This disease experience is different for patients with non-malignant diseases. Children with non-malignant diseases and their caregivers sometimes are shortly before HSCT confronted with a severe disease without any treatment experience. However, many non-malignant diseases have an inherited condition, meaning that patients were confronted with (the burden of) the illness from early childhood. The hospitalised child receives important support from their family. Caregivers are invited to actively participate in the care of their child, and during the period of transplant, a caregiver usually stays with the child for the duration of hospitalisation. The experience of HSCT should not hinder the psychosocial growth of the child and may even aid in the promotion of development and self-esteem. Nurses have a principal role in providing emotional support to the child and the family caregiver and can assist the child in understanding their condition and overcoming negative emotions.

9.1.4.1 The Paediatric Patient Experience of HSCT

HSCT is an intensive treatment process and offers the chance of a cure, but at the same time, it can generate a range of feelings including anxiety, depression, behavioural issues, psychosocial issues and post-traumatic stress reactions (Packman et al. 2010).

Many of these concerns arise from lengthy hospitalisations away from home, school and friends, isolation and an uncertain future. These factors contribute to high levels of emotion at admission and are reported to escalate until 1 week post-HSCT (Phipps et al. 2002). The paediatric HSCT patient can experience multiple hospitalisations, which can occasionally last up to 1 year or longer, depending on the severity of the complications. HSCT and its immediate and late consequences have substantial impact on the child's physical, emotional, cognitive and social well-being and consequently severely compromise the child's quality of life (QoL).

QoL

QoL is potentially affected during all stages of HSCT, including pre-transplant, during the acute post-HSCT time and during isolation and reintegration to life outside the hospital. Pre-transplant predictors of QoL include family functioning and individual resources. It is reported that during hospitalisation, children undergoing HSCT present low baseline levels of QoL. However, QoL improves as early at some months post-HSCT, returns to baseline within some years from HSCT (Tremodala et al. 2009) and is comparable for most children compared to healthy peers (Di Giuseppe et al. 2020).

Cognitive Impact

The effect of HSCT on cognitive abilities may differ depending on age at HSCT and conditioning regimens, Total Body Irradiation (TBI) containing regimes versus non-TBI. The younger the child is at HSCT, the higher the risk for deficits in intelligence quotient, academic achievement, fine motor skills and memory. The child with good cognitive developmental level at the time of HSCT can be at lower risk for cognitive deterioration (Barrera et al. 2007).

Mental Health and Emotional Concerns

Many paediatric HSCT patients demonstrate stable psychosocial adjustment or return to baseline functioning 1–2 years after HSCT. However, psychiatric morbidity in HSCT survivors is reported in some studies as higher than in the general population and appears to correlate with lower educational level and shorter post-HSCT period. Furthermore, shorter time post-HSCT, higher numbers of major infections, high symptomatology score and low educational level are predictive factors of higher psychosocial distress (Tremolada et al. 2009).

Such psychosocial distress is not unique to the immediate post-transplant period. There are concerns later post-HSCT as well. At 1-year post-HSCT, when many survivors return to school, they function at a lower academic level than what is expected for their age. They can be described by peers as absent from school more, less likely to be chosen as a best friend, less athletic and less attractive, and those who experience extensive periods of isolation may demonstrate development decline in socialisation and communication (Packman et al. 2010). There is a further possibility of long-term emotional and social behavioural problems.

Depression and Anxiety

Children undergoing HSCT are a high-risk group for developing depression and anxiety (Chang et al. 2012; Manookian et al. 2014). Contributing factors include:

- Intense medical treatments
- Single room isolation (Packman et al. 2010)
- Parental concern (Asadi et al. 2011
- Uncertainty and loss of control (Manookian et al. 2014)

Support and Fostering Healthy Coping Strategies

Transplantation should be viewed as a chance of hope for a healthy future and long-lasting happiness for the child. If the child maintains this positive attitude being hopeful about recovery, he/she can have a positive response from the treatment and overcoming complications (Manookian et al. 2014).

As expected, most children experience a sense of fear during their HSCT process. This feeling can be related to a lack of information or understanding regarding the child's condition and transplantation process. Providing clear and

understandable answers to the child's questions about the illness, treatment and prognosis can help them feel reassured and more relaxed. Information seeking is an important coping strategy for children undergoing HSCT. Developmental status and psychological state should be considered to enable appropriate communication and provision of information.

Coping strategies used to address a perceived medical or psychosocial stressor may change over time depending on personal factors and context. The child can use several different coping strategies, which are often categorised:

- Approach (i.e. information seeking)
- Avoidance (i.e. distraction or distancing)
- Problem-focused (i.e. problem solving)
- Emotion-focused (i.e. seeking emotional support)

Additionally, Bingen et al. (2012) observed wishful thinking, distraction, cognitive restructuring and social support being used both pre- and post-HSCT. Music therapy can support children during their hospital stay and can have a positive effect on experienced QoL (Uggla et al. 2018, 2019; Yates et al. 2018).

Social Support

Social support is the individual's perception of positive regard from relationships with others, the feelings to being loved, being part of a group, reassurance of self-worth and reliable alliance with others (Barrera et al. 2007). Social support is reported to be the most efficacious, for a child undergoing a HSCT, whether this is from family, friends, teachers, classmates and medical, nursing and psychosocial providers. It is both instrumental and emotional and may be provided directly to the child in the form of hospital visits or via telecommunication (e.g. video calls, phone conversation or texting, online social networking sites and e-mailing). Higher or more positively perceived social support has been identified to be associated with positive adjustment, lower distress and higher self-esteem in paediatric patients undergoing HCST (Barrera et al. 2007).

It is important for the child to benefit from sibling support. This can increase tolerance of difficult conditions encountered during the HSCT and aid in progress and recovery. During this time, they can develop deep sibling friendships, fed by a desire to be more helpful especially when the ill sibling feels lonely. When stem cells are donated by one sibling, the ill child experiences more positive feelings about him/her (Manookian et al. 2014).

9.1.4.2 The Parent Experience of HSCT

The experience of HSCT is an unfamiliar, frightening, worrying and stressful experience for the parents of the child undergoing this treatment (Asadi et al. 2011).

Several patient-centred reasons are known, including:

- Family and financial pressures
- Feelings of guilt
- Loneliness
- Hopelessness
- Fear of disease recurrence
- Transplant centre relocation
- Living in two separate households
- Commuting between home and transplant centre
- Other family member's and carer's responsibilities
- Work-related changes
- Lengthy hospital stays
- Parental informed consent for the HSCT procedure
- Medication adherence
- HSCT-related complications

During HSCT, parents develop high expectation about a successful outcome and are afraid of possible failure. The child's condition can cause parental distress, anxiety and depression. Physical, emotional and cognitive exhaustion or burnout in parents may adversely affect their ability to meet the needs of their child. They could be in extreme crisis and be unable to care for their children or perform traditional parental roles and consequently have feeling of hopelessness, concern and guilt. Parental psychological

reactions may in turn negatively affect the child. The psychological load on parents continues when the child is discharged from the ward. Burnout in mothers and fathers is associated with the child's number and severity of late effects up to 5 years after HSCT (Norberg et al. 2014). It is recommended that parents of child that underwent HSCT should be followed up and receive specialist psychological support, particularly for those whose child suffers from late effects.

The common coping strategy amongst families is with the use of social support. Parents' interactions with their support network can alleviate stress and enable parents to adapt. Some parents feel that communication with family members of other patients aids in acquiring information and in sharing of experiences and helped take control of their emotions to reduce fear and become adaptive (Badon and Cesaro 2015). Caregivers also attempt to cope by actively participating, engaging in and asking questions pertaining to their child's medical illness and the procedures involved in helping them. Parents who received cognitive-behavioural stress inoculation training in a group format had lower anxiety scores and higher positive self-statement scores (Packman et al. 2010).

Increasingly, parents function as haploidentical donors for their sick child. Being a parent and a donor creates a dual role. Depending on outcomes of the HSCT, this can be differently experienced. The dual parental role demands specific guidance and follow-up (van Walraven et al. 2012; Aguilera et al. 2022; Schaefer et al. 2022).

Creating a Therapeutic Alliance

Parents and the healthcare team need to unite to form a therapeutic alliance. Parents should be integrated into the multidisciplinary healthcare team as appropriate. The healthcare team's explanations regarding the transplant process can help them better understand their conditions and, consequently, can alleviate parental anxiety and fear of uncertainty and help further reducing their emotional burden. Parents can be supported by professionals in discussing their 'good parent' beliefs. These beliefs include personal definitions of parents on how to be a 'good parent' during the treatment process, such as in decision-making (Neumann et al. 2021).

9.1.4.3 Sibling Donor Experience in HSCT

Matched sibling donors are often preferred over unrelated donors due to decreased risk of complications. Most family members find the experience of donation as beneficial, despite some concerns about the donation process itself (Pentz et al. 2014). Sibling donors actively participate in the effort to achieve cure for their sick sibling. They have a dual role; as family members, they experience the difficulties of a life-threatening illness of one of their siblings. As donors, they are exposed to an invasive medical procedure, which adds anxiety, stress and uncertainty and places them in a complex situation (Munzenberger et al. 1999; Williams et al. 2003). When a close relationship exists between siblings, one can more safely assume that the donation will be of psychological benefit to the donor (Vogel 2011). However, sibling donors are at risk of developing emotional disturbances such as post-traumatic stress reactions, anxiety and low self-esteem and can potentially lead to the development of long-term distress responses (Packman et al. 2010). Attention should be paid to the possibility of these issues. During the pre-transplant workup, potential donors may experience anxiety and fear about the processes used to determine donor eligibility as well as during the donation process itself (Bauk and Andrews 2013). Although matched siblings may feel content and proud that they are able to be a donor, the unmatched siblings may feel inadequate or rejected and uninvolved in the transplant process. Once HLA typing has confirmed a sibling match, the workup for most haematopoietic stem cell donors involves determining both the risks to the recipient and the risks to the donor. It is also important to consider that these various tests may be overwhelming to the paediatric donor, and the importance of explaining their necessity cannot be understated. The workup process may have a significant impact on the family. In 2010, the American Academy of Pediatrics published a policy statement on children as haematopoietic

stem cell donors. Children may ethically serve as donors if five criteria are fulfilled:

1. There is no medically equivalent histocompatible adult relative who is willing and able to donate.
2. There is a strong personal and emotionally positive relationship between the donor and recipient.
3. There is a reasonable likelihood that the recipient will benefit.
4. The clinical, emotional and psychosocial risks to the donor are minimised and are reasonable in relation to the benefits expected to accrue to the donor and to the recipient.
5. Parental permission and, when appropriate, child assent are obtained. It is also recommended that the donor child will have a donor advocate or some similar mechanism, with expertise in paediatric development, that should be appointed for all individuals who have not reached the age of majority (Committee on Bioethics 2010).

The HSCT process can enhance family closeness, improve relationships with the unwell sibling and create a sense of pride and happiness about donating (Vogel 2011; Hutt et al. 2015). Wiener et al. (2007) found that younger donors focus more on the pain of the donation and tend to experience low self-esteem, anxiety and depression. Conversely, older sibling donors report lower levels of anxiety probably because they are able to think more globally about the donation process.

Studies of physical aspects and the safety of stem cell collection in paediatric sibling concluded that it is a safe procedure even in young children (Pulsipher et al. 2005; Styczynski et al. 2012). There are potential physiological risks and side effects of donation, with the most common being pain, fatigue and transient changes in the white blood count, haemoglobin and platelet values. In the immediate days following the donation, staff must closely assess the donor for evidence of bleeding, infection and other acute complications of the donation procedure. Feeling responsible for the transplant outcome is of notable concern for sibling donors. Maladjustment and poor coping in sibling donors may be attributed in part to a lack of information about the transplant process (Wiener et al. 2007).

The nurse can have a significant role in decreasing the sibling donor's stress and anxiety about the impending donation. Providing accurate and age-appropriate information about the procedure, the nurse may also help the child prepare for the experience and adapt to it more rapidly. This information increases the predictability of frightening medical procedures, thereby increasing the probability of a less stressful experience and a more rapid recovery. The nurse can also create opportunities to express emotion, concerns and questions in order to manage anxiety and guilt, involve parents in the donor's preparation and follow-up to ensure family's communication during HSCT and organise a tour of the hospital and an introduction to staff.

9.1.5 Centred Nursing Care of Patients and Caregiver's Undergoing HSCT

Psychological and emotional aspects of the paediatric experience are complex and intricate. Health workers who take care of the sick child should be the privileged listeners of the child and be receptive to the child's point of view, creating opportunities to talk.

9.1.5.1 The Relationship Between Nurse, Caregiver and Child

The approach of the paediatric team is strongly characterised by interpersonal and communication methods that are centred on empathic understanding, smiling, patience and gentleness. The relationship between nurses and children, but especially amongst nurses and parents, is difficult to summarise. However, this triangulation involves many mechanisms, roles and functions and impact on different aspects of personality and character.

9.1.5.2 Nursing Involvements in Care of Children Undergoing HSCT

To employ an effective communication, professionals need to improve their listening and obser-

vation skills and exercise the ability to transmit ideas and feelings to others.

Information and Reassurance

It is through age-appropriate dialogue that healthcare professionals can explain to the sick child the sense of what is happening, the need for frightening interventions, recognition and meaning of fears. The child must know that they will never be left alone and nothing will happen that was not first controlled or decided by someone else in whom they are confident (Manookian et al. 2014).

The opportunity for the child to be properly informed allows them to become aware of what is happening to him in his life, to have greater familiarity with hostile hospital setting and be able to work together in their treatment path. Communication about the transplant process between the care staff, child and family can be further complicated by the different opinions with respect to what it is to be explained to the sick child. In general, it is preferred to adopt an attitude that respects the will of the parents, but this can lead to difficulties when it is the child themselves asking or looking for other information. The information, however, allows a reduction of the perception of pain, an increase in the child's compliance and a general improvement of the quality of life in the hospital (Badon and Cesaro 2015). The child who reports more free expression of emotion in their family in turn experiences lower levels of distress throughout the transplant period. Openness and honesty in communication in the family environment can encourage the emotional well-being of the child and further promote their resiliency after the HSCT procedure is complete (Packman et al. 2010).

Listening

The ability to listen allows us to establish constructive relations. A real attitude to listening implies the attention, interest, tolerance, understanding and acceptance of the other. All of these are necessary preconditions for the establishment of an open relationship in which it is easier for the child to express and give information about himself. It is useful to encourage the patient to express themselves freely because, in addition to containing their distress, it is possible for the nurse to better understand the organisation of their personality and the defences put into place to cope with the situation (Badon and Cesaro 2015).

Psychological Support Service

Psychological support services are well developed and considered the standard of care in paediatric HSCT settings. Psychological support is configured, therefore, as the accompaniment's relationship of an entire family system in all phases of the transplant path. The presence of psychologist with the child who undergoes HSCT:

- Enables meaningful relationships to develop
- Facilitates understanding the illness of the child in all its complexity
- Makes request for help, expressed or implied, in view of practical difficulties, organisational, relational and emotional that may arise.

The intervention must be thought according to age, and even if the parent is always present in the isolation room, one can try to find some private moments between patient and psychologist. The attention to psychological and psychopathological aspects is not realised only through specialised interventions, but it must be realised every day by all staff members. Even the nursing staff, if trained, may perform work in the role of counsellor or coach (Barrera et al. 2007).

9.1.5.3 Decision-Making

An essential part of the treatment and care for children undergoing HSCT and their caregivers is decision-making. Several decisions about treatment and care will be made, starting with the decision for HSCT. Parents can experience HSCT decision-making as a physician's guided plan, which they follow (Pentz et al. 2012; Mekelenkamp et al. 2020). For others, the decision is approached or experienced as a more shared model, such as in sickle cell disease (Bakshi et al. 2017; Khemani et al. 2018; Mekelenkamp et al. 2021). As an

HSCT is an intensive treatment including possible severe risks, it is important to discuss personal preferences for current and future care with children and their caregivers. Spending appropriate time to discuss all options, including its pros and cons, is necessary, followed by a conversation about preferences and values, to include these into the decision.

9.2 Transplantation Through the Ages: Adolescents and Young Adults

9.2.1 Introduction

In the years that follow the onset of puberty, a young person will undergo perhaps the most rapid and formative changes of their life. The journey of transitioning from child to adult can be severely impacted when undergoing hospital treatment for a HSCT. Adolescent/teenager or young adult patients present health professionals with a unique set of challenges, and it is important that care settings are designed to address and respond to the particular needs of young people and their families. The definition of an adolescent/teenager or young adult in healthcare settings varies globally. In the UK, adolescent and young adults (AYA) or teenage and young adults (TYA) are considered between 13 and 24 years or 16 and 24 years of age; however, in some countries, it can include people in their 30s. A cancer diagnosis in young people is rare, representing less than 1% of all new cancers in the UK, but it is the second leading cause of death in this age group (TCT 2016). Numbers have grown by 10% since 1990 but have remained stable in the past decade (Cancer Research 2022). Cancers in this age group present differently compared to children and older adults and can be more difficult to treat. The infrequency of an AYA with cancer presenting to local services causes delays in diagnosis—Healthcare Professionals do not recognise the red flags (NHS England 2013). AYAs require support tailored to this age group; treating them within paediatric or adult services does not address their holistic. In response to this, guidance such as that published by the National Institute for Health and Care Excellence (NICE) aims to shape services and care to the needs of the TYA patient, which spans the ages of 13–24 years old (National Institute for Health and Clinical Excellence 2014). Patients undergoing HSCT require long-term clinical care beyond the acute phase of transplant and will be in regular contact with transplant clinicians and the multidisciplinary team (MDT) for a significant amount of time after bone marrow recovery and discharge from inpatient care. Care must be delivered within age-appropriate surroundings by health professionals experienced in caring for AYAs.

9.2.2 Special Indications for HSCT in AYA

The most common indication for HSCT is in the treatment of malignant haematological diseases lymphoma and acute leukaemia (Sureda et al. 2015). For patients with non-Hodgkin's lymphoma, acute lymphoblastic leukaemia or acute myeloid leukaemia, HSCT will be considered if they have high-risk, refractory or relapsed disease. In the case of Hodgkin's lymphoma, guidelines for teenagers indicate avoiding HSCT if the patient manages to get into complete remission (CR) following first line of chemotherapy as this alone or combined with radiotherapy usually yields successful long-term outcomes. However, once a patient requires second- or third-line treatment, the need for HSCT becomes more important (Sureda et al. 2015). Standard recommendations are for an autologous transplant following successful CR after second-line treatment. Failure to get into remission at this stage opens up the possibility of allograft, but this would require further discussions at local MDT meetings. Full-intensity allografts are more routinely used in the younger adult patients as opposed to the older population as they tend to not have comorbidities associated with getting older, e.g. heart disease, and as such can tolerate stronger conditioning.

A small number of HSCTs are carried out every year for solid tumours. According to British

Society for Bone Marrow Transplant (BSBMT) data, there were 117 transplants carried out on solid tumour patients of any age in 2020 within the UK and Ireland, all of which were autografts (BSBMT 2020). The most common solid tumours for which HSCT is indicated include neuroblastoma, germ cell and Ewing's sarcoma, with clinicians using transplants to increase dose intensity although this is reducing as other lines of treatment open for these diseases (Gratwohl et al. 2004).

9.2.3 Considerations for Care

9.2.3.1 Risk-Taking Behaviour and Non-compliance

Becoming a teenager can herald a time of risk-taking behaviours as adolescents push the boundaries of their growing independence. At a time when peers are being afforded greater freedoms, often, a cancer diagnosis re-establishes the dependency relationship between the young person and their family. Smoking, drinking alcohol, use of recreational drugs and engaging in unsafe sexual practices can allow the young person to regain some control, as can determining how compliant they choose to be with treatment. In the context of HSCT, indulging in unsafe behaviours can increase the risk of organ toxicity and infections. Failing to comply with supportive medications such as anti-infectives and immunosuppressives increases the morbidity and mortality rate of HSCT. As teenagers often focus on short-term outcomes and if the effects of non-compliance are not immediately obvious, this can reinforce the behaviour. Similarly if there have been immediate side effects to therapy, e.g. nausea and weight gain, the patient may be less likely to adhere to medical advice. This will have an effect on the success of treatment; patients who are compliant are almost three times more likely to have a better outcome than those who are not (Taddeo et al. 2008).

Gender, socio-economic status and ethnicity do not have an impact on whether a patient adheres to care (Kondryn et al. 2011) although financial difficulties can affect patients travelling long distances for treatment. Depression and lowered self-esteem can increase rate of non-compliance, as can the perception of the illness severity. The relationship between the patient and their family can impact on how compliant a young person is, with family conflict increasing the risk of non-adherence. Young patients who are treated in specialist young adult ward are more likely to be compliant compared to those who are treated in an adult cancer unit, further supporting the development of clinical areas dedicated to the care of the adolescent and young adult. This will be discussed further in the chapter.

Health professionals should be aware of the signs of non-compliance and facilitate an open and honest conversation with the patient. Confidentiality should be respected although in the instances where risky behaviour is disclosed, patients should be made aware if it is necessary to inform other members of the team or external agencies. Healthy lifestyle choices should be promoted but within a non-judgemental environment. It is important that young patients are aware of appropriate boundaries whilst in hospital and local conduct, and operational policies must support staff in challenging risk-taking behaviours within the care environment (TCT 2012). Healthcare professionals who are struggling to get their patients to comply should present the case to psycho-social MDTs for a full discussion.

9.2.3.2 Fertility

Fertility has been covered elsewhere in this book, but there are challenges unique to this age group, which will be addressed in this section. TBI and high-dose conditioning chemotherapy are highly likely to cause infertility. As often the type of transplant for the TYA patient is a full-intensity approach, this makes the risk of infertility a likely side effect of transplant. If applicable, patients must be advised about the options of fertility preservation as part of transplant workup and given the opportunity to explore fertility preservations options although the urgency of the transplant may make this difficult.

Johson and Kroon (2013) found that as many as 54% of oncologists did not discuss fertility

with AYA patients. Barriers to communication include a mutual awkwardness between the TYA patient and health professional when it comes to the topic of fertility. Clinicians can employ a jocular approach to young patients and find it difficult to broach sensitive topics (Quinn et al. 2009). Patients can feel confused and frightened about the potential effects of cancer treatment, or they are unable to envisage how fertility issues will impact them in the future (TCT 2012).

For post-pubertal males, fertility preservation can be achieved through obtaining a sperm sample. Prior to attending fertility sessions, it should be clearly explained that the sample is obtained through masturbation, so they are prepared for the process. Sperm banking can potentially be an embarrassing process. Failing to bank a sample can leave the young person feeling disappointed and letdown, and it should be reinforced that not all attempts at sperm banking are successful particularly in the context of a high burden of disease.

Female fertility preservation is a more complex process. Ovarian stimulation and oocyte collection may be considered, but currently, such methods have yielded limited success. Embryo collection can be difficult in this age group as they are unlikely to be ready to consider their current partners as a potential lifelong spouse (Levine and Stern 2010). Furthermore, there is the added issue of time as it can take 2–4 weeks to harvest reproductive material from females. An option for other cancer treatments is the use of a gonadotropin-releasing analogue hormone, triptorelin, to suppress menstruation, reduce toxicity to fertility and reduce haemorrhage risk. In other cancer treatments, it has been shown to reduce ovarian failure, but in the HSCT population, this is less successful. Female patients should partake in a full discussion about fertility preservation and be offered the opportunity to be referred to fertility experts as part of HSCT workup.

Discussions about fertility preservation should take place as early as possible, and parents should be included in order to support the teenager in their decision-making. Psychological input should be offered, as infertility can be one of the most impacting aspects of long-term survivorship, and there are many cultural, religious and social stigmas attached to being unable to bear a child.

9.2.3.3 Impact of Treatment on the Family Unit

Healthcare professionals looking after the TYA population must also care for the family unit and approach care holistically. During the ages of 13–24, young people undergo many developments in relation to the family unit. They may still be dependent on their parents, or they themselves may have their own children and responsibilities. Care needs to be adapted accordingly.

With TYA patients who are parents, often, children will be babies and preschoolers. Moore and Rauch (2006) described what parents can expect from this age group in the context of a cancer diagnosis; even with age-appropriate explanation, under 5s will have little awareness of the diagnosis and aims associated with HSCT. What they will be aware of is the absence of a parent, stress in the household and changes to their routine. Rather than understand that these are caused by illness, the child may believe that they are somehow responsible for the absence. Parents may also recognise regression in the child's behaviour, such as bed-wetting in previously toilet-trained children.

Parents of HSCT patients can find their relationship health with their partners placed under considerable strain. In Long and Marsland (2011) study, the authors noted that the needs of the parents were put on hold to prioritise the needs of the TYA patient. In the case of hospitalisation, separation between parents places even further strain as there is a decrease in communication, interaction and closeness between spouses. Reaction to the treatment process can vary between partners. One partner may try to withhold emotion to remain strong for their families, leaving the other feeling quite isolated. Differences in approach can cause emotional distance and feelings of loneliness. However, in some partnerships, going through the experience of having a child with cancer can make the partnership stronger, with spouses being viewed as the main source of support.

Siblings of young cancer patients experience chaos within their family lives, which affects family dynamics and their self-esteem (Yang et al. 2013). Siblings should be considered in the discussion about HSCT. They may need input from psychologists or youth support workers to help them adjust to the changes in their family dynamics. Spending time with an unwell sibling can increase empathy from the well child and improve the family relationship. Centres caring for TYA should encourage a family environment and include siblings in activities where possible.

Unlike other areas of medicine, family members may be directly involved in the treatment of HSCT patients by becoming the stem cell donors and as such a second patient. Siblings are usually the first option for a stem cell source. This can create an ethical dilemma for parents and healthcare staff, especially if the potential donor is a minor. What if the child refuses? What are the limitations of parental decision? What are the consequences for the child who does donate? The Human Tissue Authority provides guidance on consenting a minor for stem cell collection in their 2017 guidelines (Human Tissue Authority 2015).

There is a significant potential for psychological impact on those siblings who undergo HLA tissue typing, regardless of whether they actually turn out to be a match or not. In Macleod et al. (2003) study, siblings reported feeling as if they had 'no choice' about being tested and donating if matched. Reluctance was often not because they did not want to help but rather the fear of the procedure. In the case of siblings who were not matched, they described feelings of relief but also guilt. If they were matched but the sibling died during or post treatment, donors felt angry and blamed themselves, especially in the context of graft failure or graft-versus-host disease. Siblings in Pentz et al. (2014) study felt that there was no choice but to donate if they were matched, and concerns centred initially more around the procedures associated with donation. More than half interviewed felt they had benefited from giving their cells although they could have been provided with more information.

A further family stem cell source is the parent. In the case of failing to find a suitable donor through siblings or the register, often, parents will make a motivated stem cell donor. However, as in the case of the sibling, parents can also be left with profound feelings of guilt if the transplant fails (Barfield and Kodish 2006).

Health professionals have a duty to care for the family as a unit. Healthcare professionals should guide patients and their families on appropriate open communication although needs will vary depending on the family. Donors, whether siblings or parents, should be involved in the HSCT process from the start, and the complex variables associated with transplant success be carefully explored. Members of the MDT, such as psychologists, youth support workers, school teachers, social workers, etc., should be involved early in the journey with patient consent. Creating a family-friendly space in the clinical environment will encourage children and siblings to visit. Key workers should be aware of support networks and resources locally to refer or signpost as appropriate.

Case Study

A 14-year-old girl was treated in a TYA unit for acute lymphoblastic leukaemia. From an early point in treatment, it was clear that disease was high risk from unfavourable cytogenetics and poor response at disease reassessment. She was placed on chemotherapy but experienced complications including methotrexate encephalopathy and drug reactions to asparaginase and the alternative, Erwinase. Treatment was suboptimal. The clinical team decided to test her brother and sister to plan for a sibling allograft when a repeat bone marrow showed a significant amount of minimal residual disease after 6 months of treatment. Her sister was found to be a 10/10 HLA match. However, her mother struggled greatly with the fact that her 'healthy' child would be put through procedures, especially as she was only 10 years old. The younger child was clear on her intention to help her sister but did experience distress when subjected to blood tests. This exacerbated the inner turmoil felt by her mother as she worried about the eventual bone marrow harvest and openly discussed refusing consent for the procedure in front of her 14-year-old daughter, despite

knowing that finding an alternative stem cell source was unlikely as the patient was from a mixed ethnic background. With the help of the available psychological team and youth support workers at the paediatric and TYA centre the patient, her sibling, mother and family received separate counselling and access to play specialists and youth support workers, and the resulting harvest was successful.

9.2.3.4 Body Image

Side effects of drugs used in the HSCT process can cause significant physical changes to a patient's appearance. This is not exclusive to the TYA patient but can be more psychologically harmful as they are at an age when feeling different from peers can have a negative impact on self-esteem (Smith et al. 2012). Issues such as weight gain and alopecia can have a psychological impact, which is greater compared to the older adults. Appearance concerns amongst TYA cancer patients have been linked to depression, anxiety, feelings of loneliness, suicide and decreased treatment compliance (Fan and Eiser 2009).

Weight loss is often a part of the acute and recovery phase of HSCT as patients struggle with the gastrointestinal side effects of treatment. Traditionally literature on body image has focused on the female perspective, but for young men, muscle wastage that comes with prolonged hospital treatment, paired with fatigue, poor appetite and reduced exercise tolerance, can leave the patient feeling deconditioned. In Rodgers et al. (2010) study, participants described reduced appetites until day 50 post-HSCT, by which point, they were able to see an improvement, and by day +100 appetite was notably increased. Participants were able to correlate the link between improved eating habits and appetite with returning to their 'normal selves', advising future patients to have some control over what they eat and portion size rather than being forced into eating by parents and health professionals.

For patients receiving high-dose steroids, for example, in the treatment of graft-versus-host disease, a typical side effect includes development of facial swelling, known as 'moon face' and unwanted facial hair. This can drastically alter appearance and be devastating for a young person. This can also lead them to become non-compliant to the treatment with poor consequences for their treatment success.

Alopecia is a common and well-known side effect of chemotherapy. Hair is often very much tied into identity, and the idea of losing it can be extremely distressing at any age. Youth support workers and nurse specialists can help organise a replacement before hair loss starts to occur (usually 2 weeks after the start of chemotherapy). Wigs made of real hair can be much more realistic compared to synthetic versions. However, a lot of hair replacement focuses on females, with male patients finding options to be limited.

Conditioning regimens containing TBI can impact on the growth of patients who are treated at a young age (Jackson et al. 2018). This is due to the radiation administered to the hypothalamic-pituitary axis and the resting reduction to the growth hormone. Poor growth is further compounded by chronic GvHD, corticosteroid use and malnutrition (Chow et al. 2016). Replacement therapy can aid to reduce further loss of height, but cannot reverse loss. Clinicians need to carefully monitor growth of patients to ensure early intervention.

9.2.3.5 Impact on Life

Approximately 60% of children and adolescents who are long-term survivors of HSCT experience late effects, both of the physical and psychological nature (Forinder and Posse 2008). Fertility and growth issues have been covered already in this chapter, and organ toxicity associated with HSCT is written about in other sections of this book. There are other ways that HSCT impacts life, which are unique challenges to the AYA patient.

For the adolescent and young adult, peers are an important feature of life. However, patients of this age undergoing HSCT experience social isolation from their friends and community. This is not only due to physical absence from school, university and work but also a difficulty on the part of the healthy young person to understand and empathise with the experiences of their

unwell friend (TCT 2012). From the perspective of the survivor of a HSCT, they can find it difficult to relate to their peers after what they have been through. Young people can feel that undergoing such serious medical treatments changes their perspective on life and makes it harder to relate to peers (Forinder and Posse 2008). Also they become conscious of their change in appearance and upset at looking different to those in their social network, which can cause further alienation.

The relationship between the parents and the unwell adolescent is difficult to navigate. Increased dependency is at odds with the need for autonomy that is typical at this age. This can lead to direct conflict between the two parties, especially once the AYA patient has completed the acute phase of the transplant. A sharp difference of priorities can exist between parent and patient (Grinyer 2009). AYA patients may not have fully developed executive function due to regression and cognitive development delay, which adds to the tension between the parent and patient relationship (Kaufman 2006).

Survivorship is a growing area of research as outcomes from cancer treatment improve. Health professionals and researchers recognise that completion of cancer treatment is the start of a difficult journey of adjustment and transition. Clinical staff need to consider the fallout of treatment, and patients should be aware that they can continue to access support. Treatment within dedicated TYA clinical areas can help patients access peer support, which is tailored more to their development needs.

9.2.4 Teenager as a Child vs. Adult

Under 18s present legal challenges for healthcare professionals as the young person must be assessed on their ability to make appropriate decisions about their care on an individual basis. In the following section, issues of consent, confidentiality and guardian roles are discussed. Much of this part will discuss current legislation within the UK. Health professionals should refer to national legislation for further clarity.

9.2.4.1 Consenting for Treatment

Informed consent is a cornerstone of medical practice. Violation of this has legal implications for clinicians but more importantly jeopardises the ethical rights of the patient (Bayer et al. 2011). In order to satisfy the principles of informed consent, it must be given freely and with full comprehension. Patients must be provided with adequate information in understandable terms. Treatment options should be reviewed, and a discussion about the risks, benefits and alternatives to the proposed treatment should take place and be documented. Signing of a consent form is symbolic, representing completion of the consenting process.

Informed consent is a relatively straightforward process when concerning over 18s as long as the individual has capacity. In the UK, patients between 16 and 18 can consent for treatment but may not be able to refuse treatment in the case of saving their lives or preventing serious harm. Under 16s may legally consent if they meet certain criteria of being Gillick competent. This principle is based on a case in the 1980s where Victoria Gillick took her local authority to court to prevent them from providing contraception to her children without her knowledge (Wheeler 2006). The high court determined that minors under 16 have the potential to independently consent to treatment if deemed competent to do so. However, it is a good practice to involve the young person's family in the process. In the case of under 18s who are deemed Gillick competent but refusing treatment, it is possible for the decision to be overturned where it will lead to death or serious injury (Department of Health 2009).

In the case where a minor cannot independently consent and parental involvement is required, the Oviedo Convention recommends the use of the term 'authorisation' rather than 'consenting on behalf of a child' as the former relates to the concept of a third authority, i.e. the parent, and is slightly different from informed consent. As informed consent is an expression of personal choice, it can only relate to the person being treated. Authorising treatment is acknowledging that it is in the best interests of the young person. Furthermore, the Oviedo Convention

requires that the opinion of the minor must still be taken into consideration. Thus, the decision-making process involves three parties: the clinicians, the person with parental responsibility and the child undergoing treatment (Nicolussi 2015). According to the Children Act 2004, parental responsibility extends to both parents if married at the time of conception or birth, the child's father if not married to the mother but who features on the birth certificate or the child's legally appointed guardian or a local authority who has been granted a care order in respect of the child.

Disputes between parties involved in treatment decisions are rare but do occur. This can be between patients and their parents, between health professionals and the family or between parents. An example is when parents who are Jehovah's Witnesses refuse blood transfusions on behalf of their child. Cultural beliefs should be respected, but bone marrow failure can be a life-threatening complication of HSCT. In instances such as this, which can be pre-empted, plans should be made about how to deal with the complication before it arises, i.e. the use of erythropoietin as an alternative. Unfortunately, not every eventuality can be considered, and advice may need to be sought through legal channels, which will provide protection to the patient, family and the health professionals concerned.

9.2.4.2 Communication

Regardless of whether a minor is able to consent, they should be present to participate in discussions about their care, and information should be directed at them. Healthcare professionals should give the same time and respect to young people as they would do to adult patients. Information should be provided using language that is understandable, giving all involved parties the opportunity to ask questions. Discussions should be truthful and open, with consideration given to confidentiality. The information provided should be appropriate to the age of the young person and include a discussion about:

- Their illness and proposed treatment
- The purpose of investigations and treatments and what they involve
- Benefits and risks, including of not having treatment
- Who will be responsible for their care
- Their right to ask for a second opinion or retract consent if deemed capable (GMC 2007)

It is justifiable to keep the above information from the young person if you think that it will cause them serious harm (this does not include concerns about upsetting them) or if the patient asks you not to tell them, preferring to leave someone else to make the decision for them. The treating team should continue to revisit this decision by the young person as participation in their care will enable them to better process their treatment journey.

Often guardians and young people can struggle to have honest discussions together as they are afraid of upsetting each other especially in the context of sensitive subjects. Although the young person is entitled to have consultations on their own, it is better if they can be supported by somebody as the HSCT journey can be difficult and lonely. The MDT are in a position to break down the barriers of communication and help the young person and their support network navigate this difficult time.

9.2.4.3 Confidentiality

Respecting confidentiality is important in harbouring good relations with young people, making them feel confident about seeking care and advice. If required to share information with parents or other health professionals, the young person should be made aware and agree. If they refuse, there are still circumstances where information should be disclosed including where it would be in the public's best interest, when it is in the best interests of the young person, when they lack capacity and when disclosure is required by law. Examples include if the information would help prevent or prosecute in the case of a serious crime (usually against the young person) and if the patient is engaging in activities that might put them at risk, e.g. serious addiction or self-harming.

9.2.5 TYA Cancer Care in Europe: A General Review

Across Europe, cancer is the second cause of death amongst 15–24-year-olds (Gatta et al. 2009). Despite this, the services for this population remain in the developing stage in comparison to that of children or older adults. This is a strive for change, and an example of this is the European Network for Cancer Research in Children and Adolescents (ENCCA) programme, which aims to share knowledge and services across the continent. Stark et al. (2016) summarised the work across individual countries and set out guidelines with collaborative aims to:

- Not necessarily have agreed age cut-offs set across Europe, rather treat according to the needs of their population
- Provide an age-appropriate environment for TYA patients to complete their care, with services tailored to the needs of the patient and family
- Have an active relationship between paediatric and adult oncologists or a dedicated TYA team, including specialist health professionals such as nurses, social workers, psychologists, teachers and activity coordinators
- Have a fertility preservation programme
- Have a transition programme for those moving from child to TYA services and TYA to older adult care
- Have clinical trials available to the TYA population in varying tumour groups

Stark et al. (2016) also summarised progress of individual countries in regard to TYA care.

The UK pioneered the TYA model back in the 1990s through collaboration between the Teenage Cancer Trust (TCT) and National Health Service (NHS). As such, the pathway is well defined. All TYA patients with a cancer diagnosis must be discussed at a TYA MDT, and those between 13 and 18 must be treated in a dedicated TYA centre. The service undergoes yearly peer review, and lead clinicians are at the forefront of specialist networks. There is a separate TYA clinical studies group with the aim of including the availability of trials to this patient group. TYA health professionals have their own UK professional membership organisation, which provides peer support and sharing of information between services. There are 25 TYA centres across the county, and development of such services is discussed in detail in the next section.

In Germany, there is separate infrastructure for paediatric and adult cancer patients with a strict age barrier of 18 years separating them. The majority of adolescent care is performed within paediatric oncology. However, practice is changing, and a collaborative approach is happening, with some centres creating TYA-specific MDT programmes.

In Italy, the Committee on Adolescents was formed by the Associazione Italiana Ematologia Oncologia Pediatrica in 2010 to ensure TYA cancer patients have prompt, adequate and fair access to the best care. Since then, two TYA units have been opened. A national task force dedicated to teenagers and young adults with cancer was set up in 2013 to push the agenda for TYA care further.

In France, research by Desandes et al. (2012) showed that 82% of 15–18-year-olds with cancer were treated in an adult environment, and few were enrolling clinical trials. This prompted the initiation of an improvement plan. Since then, eight TYA units and three specialist centres have been opened with dedicated teams; improvements have been made to the inclusion of TYA patients in clinical trial, and a specific psychosocial programme has been initiated. The Institut de France planned to create localised care pathways and has started a national association to focus on cancer care for patients between 15 and 25 years old.

In Spain in 2011, the Adolescents with Cancer Committee was set up by the Spanish Society of Paediatric Haematology; however, a survey in 2014 showed that over 14-year-olds were still generally being treated in adult care settings (Lassaletta et al. 2013). TYA oncologists and patients have founded the charity 'Spanish Association of Adolescents and Young Adults with Cancer' to create support for young people with cancer and push the TYA agenda.

In Denmark, a TYA project started by nurses commenced in 2000 at Aarhus University. A national initiative is also being planned to bring together the collective view of young patients, to create TYA-focused unit and to specialise treatment.

In 2013, in the Netherlands, health professionals started a national TYA project dedicated to the care of 18–35-year-olds and focused on quality of life, late effects and fertility.

In Portugal, there is no national project yet, but in Lisbon, a project has commenced to create a TYA unit for patients aged between 16 and 25.

9.2.6 Development of TYA Cancer Units: The UK Experience

It was first recognised that young UK patients had specific needs in the 1950s with the publication of the Platt Report (Ministry of Health 1959). Publication of the Calman-Hine report in 1995 particularly acknowledged the issues faced by young cancer patients. Treating 13–18-year-olds in the same units as toddlers or over 18s with older adults fails to provide care that meets their needs. The UK has been at the forefront of developing TYA-specific treatment areas; however, age-appropriate care is still not available to all.

The Teenage Cancer Trust charity was set up over 10 years ago to act as support and advocate for young people facing cancer. Alongside other charity organisations internationally including CanTeen Australia, CanTeen New Zealand, LIVESTRONG and SeventyK, they created the International Charter of Rights for Young People with Cancer, which states that young people with cancer should:

- Receive education about cancer and its prevention
- Be taken seriously when seeking medical attention to ensure that they receive the earliest possible diagnosis and referral for a suspected cancer
- Have access to suitable qualified health professionals with significant experience in treating patients with cancer in this age group
- Access to suitable clinical trials
- Receive age-appropriate support
- Empowered in making decisions
- Fertility preservation
- Access to specialised treatment and services in age-appropriate facilities
- Financial support
- Long-term survivorship support

The Teenage Cancer Trust was set up over a decade ago and works in partnership with the National Health Service to open inpatient and outpatient cancer units, providing education, specialist staff and annual meetings to raise awareness of the issues associated with caring for this age group. In 1990, they opened the first dedicated unit at the Middlesex Hospital in London and currently have 28 units operating across the UK. Development of TYA-dedicated units is down predominantly to initiatives in response to local needs rather than a general coordinated health policy.

During the development stage of a new unit, often, patients will be asked for their opinion and input into the facilities and design. Use of the Internet is important in this age group as a means of staying in touch with normality whilst staying in the hospital, so facilities should be provided. Patients have access to equipment such as game consoles, pool tables, computers, etc. Designated recreational areas can provide a space for patients to socialise and relax away from their hospital beds. This can also encourage peer support as patients interact in communal spaces. Support for the young person can be gained by having somebody staying with them, and clinical areas should be able to accommodate. This is often possible in paediatric and teenage settings but can be difficult to provide in adult units.

The ethos of AYA care is to approach holistically. This is achieved by presenting each new patient at weekly AYA MDTs. During AYA MDTs, health professionals from across the service attend to participate in discussions about new patients and their planned treatments. All AYA patients, irrespective of place of treatment, should be discussed at an AYA MDT to ensure that they have the opportunity to receive the cor-

rect support. Barriers to setting up a TYA MDTs, including time constraints, perceived duplication and resources (TCT 2012). However, uses of MDTs are thought to improve clinical trial recruitment, outcomes and multi-agency working.

Due to duration of follow-up post-HSCT, patients may be required to transition as they pass landmark birthdays. This should be a planned process that addresses the needs of TYA patients with chronic health problems as they move from child-centred care to the TYA setting or TYA care to the adult health system. This can be a difficult time for patients and their families as they leave behind the team that has moved them through the acute phase of the HSCT process and with whom they have built up a strong bond. Planning may take a number of months and should be approached sensitively. The process can be helped by patients visiting the new units and good communication between all parties.

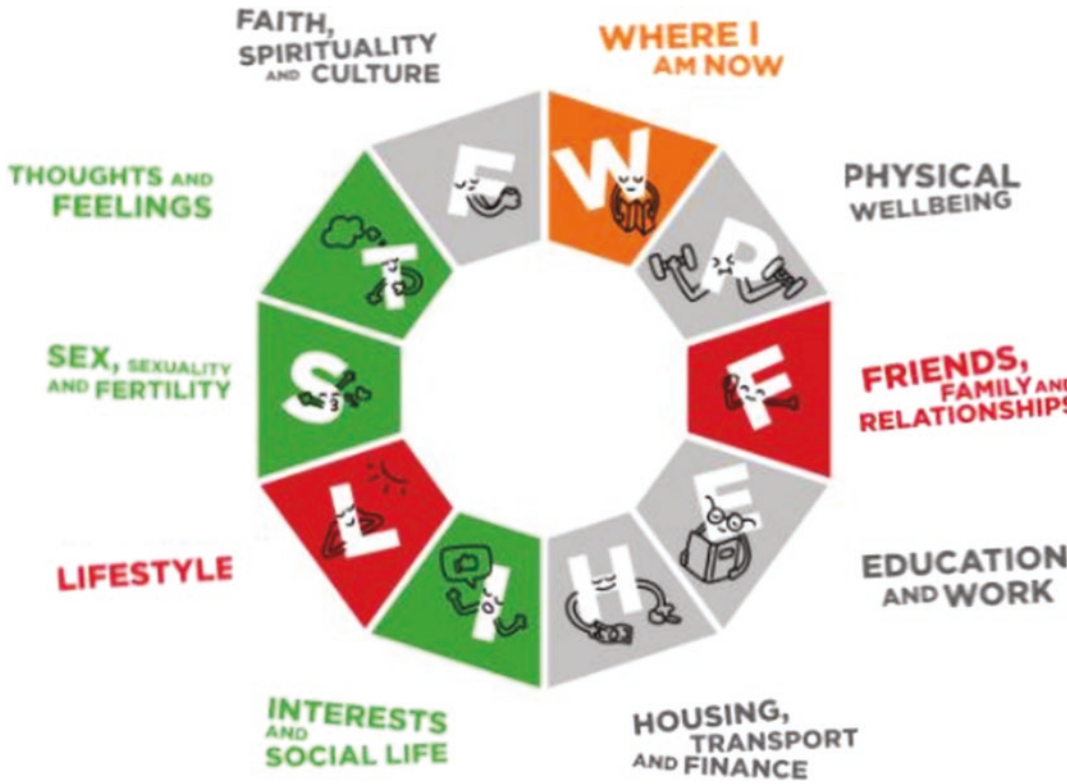
9.2.7 AYA Care: An MDT Approach

In the UK, AYA care occurs within networks. Within each network, there is at least one principle treatment centre (PTC), which works with other hospitals (termed designated hospitals) to ensure that young people can access care both in specialist centres (PTC) and in the hospitals closer to them, saving on the time and cost associated with travelling for appointments. Previously, the relationship within the network was governed by loose principles, which were hard to audit and govern, but in 2022, NHS England has worked with AYA Teams to create service specifications for AYA cancer care in PTCs and designated hospitals. This will formalise the networks and work to ensure that all AYA patients across the UK receive standard supportive care once diagnosed with cancer.

The service specifications include recommendations on (amongst other things):

- Tumour banking
- Availability of whole genome sequencing
- Improve access to clinical trails
- Appropriate care according to age and diagnosis
- Holistic care of AYAs
- Fertility
- Survivorship
- Transitioning through paediatric and adult services

One recommendation is that all AYAs being treated for cancer across the Network must be discussed at a psycho-social MDT, hosted at the PTC and attended by medics across the typical AYA tumours, specialist nurses, psychologists, social workers, youth support worker, trials researcher or nurse. The barriers to setting up a TYA MDTs include time constraints, perceived duplication and resources (Smith et al. 2012). However, use of MDTs is thought to improve clinical trial recruitment, outcomes and multi-agency working. Each patient is discussed using the Integrated Assessment Mapping (IAM) tool. Aside from diagnosis, treatment and trials being presented, the nurse specialist will also discuss the outcome of the health needs assessment, which they have completed with the patient. This focuses on specific areas of the young person's life where they award a score depending on how much distress the domain is causing and add supplementary comments. This highlights particular areas of concern for the young person and can focus the discussion during the MDT. This is separate from the diagnostic MDT and is purely focused on the holistic needs of the young person and their families.



Found at https://iamportal.co.uk. (Reproduced with permission from Teenage Cancer Trust, 2022)

9.2.8 Summary

- TYA cancer patients include those aged between 13 and 24 years old.
- Often, HSCT indications in this age group are for malignancies including refractory or relapsed leukaemia and lymphoma.
- There are unique challenges facing this age group when diagnosed and undergoing treatment.
- One significant challenge is the impact that a cancer diagnosis has on the family unit especially in the younger siblings providing the stem cell.
- Even when considered a minor, patients do still need to be assessed for competence and afforded the same respect as adult patients.
- Partnership between the NHS and charities such as the Teenage Cancer Trust can provide an age-appropriate environment for patients and their families.
- There is still much work to be done across Europe to ensure each patient is getting care that is responsive to their needs.

9.3 Transplanting the Adult and the Older Adult: Nursing Considerations

Older people are usually identified by their chronological age, and persons aged 65 years or over are often referred to as 'elderly' (WHO 2010). The median age at diagnosis of patients with acute myeloid leukaemia (AML), myelodysplastic syndromes (MDS), chronic lymphatic leukaemia (CLL), multiple myeloma (MM) and non-Hodgkin's lymphoma (NHL) is over 65 years old (Eichhorst et al. 2011; NCI 2003; Palumbo and Anderson 2011; Sekeres 2010; Smith et al. 2011; Siegel et al. 2015). Most of these haematological diseases are not curable unless an allogeneic or autologous haematopoietic cell transplantation can be performed.

Currently the indications for and subsequently the use of haematopoietic cell transplantation as a treatment option in older adults with haematological malignancies are increasing, yet the majority of our experience is with patients under the age of 65.

Older patients however represent a very heterogeneous group with respect to overall health status; some individuals stay fit, whilst others are frail or become fragile suddenly.

In order to help healthcare professionals decide on the best treatment option for their older patients, geriatric assessment (GA) (Extermann et al. 2005) can identify unknown medical, functional, cognitive and social issues, making it possible to plan early interventions. Geriatric impairment, such as polypharmacy, malnourishment and impaired instrumental activities of daily living, is common among older haematological patients (Scheepers et al. 2020). Although GA still requires prospective validation in larger cohorts, studies in oncological populations have shown that treatment plans have been altered in 28% on the basis of the CGA, often resulting in less intensive treatment options. A substantial percentage of older adults have more difficulties processing and remembering information than younger ones. It is important to make sure that also older adults understand their disease, the prognosis and the treatment plan to make an informed decision. Therefore, it is essential to assess cognitive functioning and in case of mild cognitive impairment that the information is tailored to reflect the individual's needs. There are studies suggesting that physiotherapy and nutritional counselling might improve quality of life and treatment completion. Consequently, it would be most interesting to improve geriatric impairments or deficits. Unfortunately, most healthcare professionals working in hematology settings are not trained in geriatrics.

The aim of this section is to describe GA, to provide information about the increasing prevalence of certain risk factors (impaired cognitive function, medication non-adherence) and how patient information can be adjusted to the needs of older patients.

9.3.1 Differences Between Older and Younger Patients

The incidence of acute myeloid leukaemia (AML), myelodysplastic syndromes (MDS), chronic lymphatic leukaemia (CLL), multiple myeloma (MM) and non-Hodgkin's lymphoma (NHL) increases with age, with the majority of patients being over 65 years of age (Eichhorst et al. 2011; National Cancer Institute 2003; Palumbo and Anderson 2011; Sekeres 2010; Smith et al. 2011; Siegel et al. 2015). Most of these haematological diseases are not curable unless the appropriate allogeneic and/or autologous haematopoietic cell transplantation is performed.

Chronological age is becoming less of a barrier to reduced-intensity conditioning in allogeneic haematopoietic cell transplantation (HCT), and as a result, HCT in the older adult population is increasing. However, the majority of experience with stem cell transplantation remains amongst younger adults.

Older Age is Still Associated with

- Pharmacokinetic and pharmacodynamic changes
- An increased risk of toxicities and infectious complications from chemotherapeutic agents
- An impaired immune system
- A high prevalence of comorbid conditions and an overall worse performance status

These factors may result in higher risks of non-relapse death after both autologous and allogeneic HCT (Artz and Chow 2016; Mamdani et al. 2016).

Older patients represent a very heterogeneous group in terms of health and functioning; as whilst some individuals remain fit, others are frail or become fragile suddenly.

More than half of adults aged over 65 have three or more medical problems (Boyd et al. 2012) and may be taking multiple medications, making care more complex.

In older patients, therapeutic decisions are widely based on the patient's age, general health, the disease features as well as the patient's personal wishes and clinical judgement. However, even amongst older patients with a good performance status, geriatric impairments are reported (Scheepers et al. 2020; Extermann et al. 2005). In order to help healthcare professionals (HCP) who have not been trained in geriatrics work with older patients and caregivers to decide on the best treatment option, GA can be used to objectively evaluate patients, identifying medical, functional, cognitive and social issues, making it possible to uncover potential problem areas and plan early interventions. Although GA still requires prospective validation in larger cohorts and in the transplant setting (Elsawy and Sorror 2016), this assessment is able to predict survival and toxicities (Artz et al. 2006; Palumbo et al. 2015) and to detect unknown geriatric problems, making it possible to plan early interventions and to influence treatment decisions (Kenis et al. 2013). However, performing a GA is relevant, and recent studies in oncological populations show that treatment plans have been altered in 28% on the basis of the CGA, often resulting in less intensive treatment options (Hamaker et al. 2018). Amongst older haematological patients (even with good performance status), geriatric impairments are common (between 17% and 68%), and polypharmacy, nutritional status and IADL were the most impaired (Scheepers et al. 2020).

9.3.2 Geriatric Assessment

GA strategies need to be implemented early on in the patient pathway in order to facilitate decision-making in relation to the optimal approach to treatment. It can assist in identifying patients most likely to benefit from standard induction and post-remission therapies, as well as in the consideration of performing HCT. To determine the best treatment for the patient, GA is needed to systematically uncover medical, functional, cognitive and social issues, which may compromise the treatment. Table 9.1 provides an overview of domains and tools commonly used. Domains are assessed by means of commonly used tools to measure functional status, cognitive function, nutritional status, comorbidities, polypharmacy and socio-economic status. Some use this in combination with a short screening tool to detect vulnerability. An appropriately trained healthcare professional can perform the assessment, and in some cases, this may be a nurse. GA instruments aid in identifying potential problems; however, when the problem is identified as being severe, a thorough assessment is needed to understand the cause. In order to optimise the outcomes of the older patient, a geriatric intervention or referral may be necessary, for example, to the geriatrician, dietician, physiotherapist, social worker or psychologist. There are several studies that report that impairment of physical function, cognition and mental health, malnutrition and polypharmacy are associated with decreased overall survival (Kennedy and Olin 2021), but for healthcare professionals not trained in geriatrics, it would be most interesting to know whether improving impairments or deficits would improve quality of life and treatment completion. However, it is too early to draw conclusions, and above all, quality of life is hardly addressed in most of the studies.

A full GA can be time-consuming and burdensome for HCP who are not trained in the evaluation of older adults. The use of more simplified screening tools like the Vulnerable Elders Survey (VES) (Saliba et al. 2001) and G8 screening tool (Soubeyran et al. 2011) can be employed in an initial appraisal, identifying those who would benefit most from a more detailed and complete GA. One of the latest recommendations of the International Society of Geriatric Oncology (SIOG) reported that of 68–82% of cancer patients >70 years scored abnormal on the G8 (≤14). In addition, 74–94% of these patients were frail according to a GA (Decoster et al. 2015).

Table 9.1 Comprehensive geriatric assessment domains and commonly used tools and screening tools

Domain	Tools	Reference
Functional status	Performance status (PS)	Karnofsky and Burchenal (1949), Mor et al. (1984)
	Activities of daily living (ADL)	Mahoney and Barthel (1965)
	Instrumental activities of daily living (IADL)	Graf (2008)
	Self-reported number of falls	Peeters et al. (2010)
Comorbidities	Hematopoietic cell transplantation comorbidity index (HCT-CI)	Sorror et al. (2005)
Polypharmacy	Comprehensive drug review	
Geriatric syndromes	Mini-mental state examination (MMSE)	Folstein et al. (1975)
	Geriatric Depression Scale (GDS-15)	Almeida and Almeida (1999)
Nutritional status	Malnutrition Universal Screening Tool (MUST)	Stratton et al. (2004)
	Simplified Nutritional Assessment Questionnaire (SNAQ)	Kruizenga et al. (2005)
	Mini Nutritional Assessment Short Form (MNA)	Guigoz (2006)
Screening tool		
Vulnerable elders survey	Age	Saliba et al. (2001)
	Self-rated health	
	Six physical function limitations	
	Five IADL/ADL items	
G8 screening tool	Appetite, weight loss, BMI	Soubeyran et al. (2011)
	Mobility	
	Mood and cognition	
	Number medications	
	Patient-related health	
	Age categories	

9.3.2.1 Functional Status

An important determinant of frailty is functional status, including Karnofsky's performance status (PS) (Karnofsky and Burchenal 1949; Mor et al. 1984), the activities of daily living (ADL) (Mahoney and Barthel 1965) and the instrumental activities of daily living (IADL) (Graf 2008). The PS is utilised routinely in HCT and is a global estimate of the overall health of patients according to their doctor. The ADL measures the level of independence or dependence of patients and, in terms of limitations to self-care, mobility and being able to walk and continence status.

The IADL describes the more complex ADLs necessary for living in the community and assesses the competence in skills such as shopping, cooking and managing finances, which are required for independent living.

Evaluation of gait difficulty and self-reported number of falls may also be useful when looking at functional status. Problems may be caused by fatigue, muscle weakness, dizziness or neuropathies induced by cancer or its treatment and can cause significant mortality and morbidity.

9.3.2.2 Vision and Hearing Impairments

Many older adults have either a visual impairment, a hearing impairment or both. There is evidence of an association between hearing impairment and cognitive decline amongst older adults (Valentijn et al. 2005). An evaluation of visual and hearing acuity of any patient should be undertaken during the physical assessment. Where possible, hearing and visual impairments should be corrected, so that elders can function better, promoting greater independence.

9.3.2.3 Comorbidity and Polypharmacy

Typical older adults have multiple comorbidities. For HCT, comorbidity can be assessed by using the haematopoietic cell transplantation comorbidity index (HCT-CI) introduced by Sorror et al. in 2005, as an evaluation of organ dysfunction for potential HCT recipients. The HCT-CI was developed from the historical Charlson Comorbidity Index (Charlson et al. 1987).

Due to existing comorbidities, the older patient is often taking multiple medications—each with their own side effects, interactions and contraindications. Polypharmacy (defined as an excessive number of medication (≥5)), is sometimes further increased by medications, which can be bought

over the counter without prescription. Some of these medications may interact with prescribed cancer treatments or even supportive medications such as immunosuppressive agents that are used following HCT. A comprehensive drug review is strongly advised before initiating therapy and then regularly throughout the patients' treatment pathway to maintain accurate records of concomitant drugs and ensure avoidance of potentially inappropriate medications.

9.3.2.4 Cognitive Functioning

Although cognitive decline is acknowledged to increase with age, significant variability is noted amongst the older population (Greene and Adelman 2003). They define mild cognitive impairment as 'deficits in memory that do not impact on daily functioning'.

However, consequences of even mild cognitive impairment are significant because these patients may have more difficulty understanding the risks and benefits of treatment and also adhering to complex cancer treatment regimens. It should be remembered that a diagnosis of cognitive impairment does not necessarily mean that the patient is incapable of making decisions and consenting. Most patients are still able to understand the risks and benefits of treatment and of being involved in research. It is important that researchers do not automatically exclude patients with cognitive impairment from treatment but that every effort is made to ensure that patients are fully informed in order to be able to give their consent.

Assessment of cognitive function is included as a domain in GA. In addition, the Mini-Mental State Examination (MMSE) is widely used as a screener for cognitive impairment and for dementia in older persons (Folstein et al. 1975).

9.3.2.5 Geriatric Syndromes

Geriatric syndromes include dementia, depression, delirium, osteoporosis, falls and fatigue. Specific geriatric syndromes can be assessed with instruments such as the MMSE and the geriatric depression scale (GDS-15) (Almeida and Almeida 1999). The MMSE assesses to which degree the person is alert, oriented and able to concentrate and perform complex mental tasks and affective functions and detects signs of dementia (Folstein et al. 1975; Sattar et al. 2014). The geriatric depression scale (GDS-15) searches for signs of depression (Sheikh and Yesavage 1986; Almeida and Almeida 1999). The presence of dementia and/or depression is associated with a negative impact on survival (Pallis et al. 2010).

9.3.2.6 Medication Adherence

During HCT, it is imperative that patients adhere to the prescribed treatment. Non-adherence leads to poorer health outcomes, such as increased incidence of transplant-related morbidity and mortality, higher cancer recurrence rates and shorter survival (Puts et al. 2014).

Older age has not been identified as a risk factor for non-adherence, unless the older adult himself perceives insufficient social support. For older adults, certain factors are known to impact upon medication non-adherence. These include factors relating to the healthcare system and the treatment team:

- High cost of medication whilst patient income is low
- Incomplete insurance coverage
- Lack of coordinated care
- Individual factors such as misunderstanding of instructions, intentional choice of medication and non-adherence to accommodate the individuals' lifestyle and daily activities (Van Cleave et al. 2016)

Whilst there is no screening tool currently available for non-adherence in gero-oncological patients, there are several existing medication adherence scales available to assess patients' adherence to medication (Lam and Fresco 2015).

9.3.2.7 Nutritional Status

Nutritional deficiency and malnutrition are common in older adults. The presence of weight loss and/or anorexia points towards malnutrition, which increases vulnerability to illness. In order to determine nutritional status, screening instruments like the Malnutrition Universal Screening Tool (MUST) (Stratton et al. 2004) or Simplified Nutritional Assessment Questionnaire (SNAQ) (Kruizenga et al. 2005) are available. In all these screening instruments, unintentional weight loss

in a short time is a fixed-item parameter to evaluate malnutrition. In order to diagnose malnutrition, the Mini Nutritional Assessment (MNA) (Guigoz 2006) can be used. The MNA assesses:

- Decline in food intake
- Weight loss and mobility
- Neuropsychological problems
- Body mass index
- Number of medications taken per day
- Patients' assessment of their health status compared with others their own age

A multidisciplinary approach to nutrition assessment, care planning, intervention and evaluation in HCT patients should be advocated where possible, with the involvement of healthcare professionals such as dieticians and nutrition specialist teams in collaboration with the medical and nursing team.

9.3.2.8 Socio-economic

Social support, persons' general living conditions as well as availability and adequacy of caregivers should be an integral part of GA. There are different types of support, such as:

- Everyday emotional support
- Emotional support with problems
- Appreciation support
- Practical support
- Social companionship
- Informative support

Everyone needs everyday support in a certain way. The type and amount of support needed will depend on the individual and also the phase of the illness and treatment. Consideration should also be given to the well-being of the caregiver as the quality of life and quality of care of the patient also depend upon this factor.

9.3.2.9 Decision-Making

Older persons may have grown up in a healthcare culture where decision-making was more paternalistic. As a result, this may either lead to lower requests for information by the patient or to a risk of poor overall communication. For most young patients, the decision and desire to be transplanted are often clear. For older patients however, the decision is often far less obvious, and the choice to proceed to HCT is a complex one (Randall et al. 2016). Patients might think they are 'too old' for HCT or be concerned whether they can find an available caregiver and whether they have enough money for extra costs incurred or that it will impair their quality of life (Randall et al. 2016). Medical information about the general process and outcomes of the transplant, donor sources, medications, timelines and risks and benefits of the procedure are usually provided after induction therapy has been successful. However, older people have more difficulties processing and remembering information than younger ones (Posma et al. 2009), and cognition may have been affected further by the chemotherapy that has been given (Williams et al. 2016). It is important, therefore, to provide education about HCT, which is gradual and repeated during induction and, afterwards, presented using plain language, empowering the older patient to make the decision about transplant (Randall et al. 2016). In order to improve the patients' ability to actively participate in the decision-making process and increase treatment adherence, a step-by-step approach should be considered (Posma et al. 2009) and narrowed down to what is meaningful to make a decision (D'Souza et al. 2015; Posma et al. 2009). Regarding risks and general knowledge of medical procedures, written information, multimedia interventions, extended discussions and test/feedback techniques can improve the patients' understanding (Schenker et al. 2011). Particular attention should be paid to implementing interventions that are accessible to patients with limited literacy and/or limited vision. These groups are at increased risk for poor comprehension.

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