Transplant Preparation

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Abstract

HSCT is a complex procedure, which involves a long and complicated pathway for the patient and the intervention of many health professionals. Within this multidisciplinary team, the transplant coordinator, usually a nurse, is the 'essential marrow', the heart and the vital backbone of this procedure; they are an essential transplant ingredient facilitating a fluidity of the pathway and a good transmission of information. Written information about the procedure is beneficial for patients either prior to clinic visit or during clinic to allow the patients and relatives to reflect on conversations. Transplantation carries a significant risk of morbidity and mortality, and these should be considered regarding the 'need' to transplant, based upon risk of disease, versus risk of the transplant. Pre-transplant assess-

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ments must also be undertaken, and the results of these along with suitable donor medical clearance and cell availability are essential to ascertain that transplant is a valid option and can proceed safely. Dealing with fertility preservation upon diagnosis of cancer is often challenging; this issue is even more complex for paediatric patients. PDWP recommends that counselling about fertility preservation opportunities should be offered to each patient receiving HSCT.

This chapter will also focus on vascular access for optimal treatment of haematology patients because stem cell treatment cannot be performed without it. Constant advances in haematology have raised challenging ethical dilemmas concerning end of life, palliative care, patient information, donor concerns and impartiality and issues related to the risk we run to our patients. Nurses provide a key role in patient education, providing pre- and post-transplant advocacy and counselling, plan hospitalisations and consultations. They also act as educators and role models to nursing students and share knowledge in accordance with local policies and JACIE guidelines.

Keywords

Transplant coordinator • Nurse • Multidisciplinary team (MDT) • Ethics • Complex procedure • Venous access

4.1 The Role of Transplant Coordinator

The role of the transplant coordinator (TC) is to ensure that timely events occur for each patient and their families undergoing haematopoietic stem cell transplant (HSCT), ensuring that patients are physically and psychologically prepared for the treatment. Many transplant coordinators are nurse specialists who focus their role on the individual needs of the patient and families; however, some centres have medical staff that organise transplants. TC provide a high level of care and management, inform and educate the patient, have holistic knowledge of the patient, participate in specific or advanced nursing practices (bone marrow sampling, HLA typing, transplant recipient care) and coordinate all the transplant logistics.

The transplant coordinator ensures that a suitable source of cells is available following the high-dose chemotherapy or immunosuppressive treatment that the patient will receive.

The TC supports the patient education and coordination of all care and embodies a clinical nursing function where emphasis is placed on specialisation in a clearly defined area of care.

The TC also takes cares of the donor, to welcome and accompany the donor in his procedures: information, assessment, reimbursement of expenses and psychological follow-up.

They are involved in the creation of information tools for the patient and the donor which are evaluated in order to have an accurate knowledge of patients' needs. A TC actively participates in the JACIE process of accreditation of transplant centres by writing and evaluating SOPs.

Within the last decade, transplant centres across Europe have invested in new nursing roles allowing quality, continuity and coordination of care, providing a link between all members of the transplant team (physicians, nurses, cell therapy, immunologist, radiotherapists to name a few) and actively participating in the accreditation process.

4.2 Information and Consent

Written information is considered to be beneficial for patients either prior to clinic visit or during clinic to allow the patients and relatives to reflect on conversations (Patient Information Forum 2010). It is good practice to have had in-depth discussions with patients on at least two occasions prior to transplant consent and admission. There are many good information leaflets available for patients and their relatives to gain an overview of the procedure, some generic and others disease specific. Information should be offered to the patient early in their transplant journey where appropriate. Consent for transplant should be taken prior to admission and before the donor in allogeneic transplants starts any mobilisation therapy. Each country will have different legislation to follow, and guidelines for this will be available within your centre. Consent should be obtained by medical personnel who have received the appropriate, documented training in consenting to medical treatment and examination. Usually, for transplant consent due to its complexity and significant mortality risk, it would be considered as reasonable that this will be taken by the patient's consultant or designated deputy, to ensure all known factors and concerns are addressed appropriately.

Consent and information given to the patient should be balanced against the risk of disease. Indications and suitability of potential transplant candidates are identified, as indicated by EBMT guidelines and local policy. Yet decisions are the responsibility of medical teams with input from other members of the multidisciplinary team (MDT) based around EBMT guidelines; however, the patient needs to be in agreement and fully informed of the process, and the final decision should be with the patient, with appropriate support and guidance.

During the consent process, patients should be informed of the reason for transplantation and the risks and potential benefits associated with the procedure; this will vary depending upon conditioning, individual risk factors and the donor chosen. Information should include (but not be exclusive to) the risk of graft versus host disease (GVHD), infection, bleeding, multi-organ damage/failure, infertility, hair loss, pain and possibility of death.

Consent for data collection is also important and is in line with the data protection act since 1998 and allows EBMT to collect anonymous information about the transplant, disease groups and outcomes, enabling future developments, trends and research opportunities. Patients should provide consent for their centre to send this information.

4.3 Information and Consents in the Paediatric Population

Informed consent is an essential part of healthcare practice. Parental permission and childhood assent is an active process that engages both adults and children, in their health care. Paediatric practice is unique in that developmental maturation allows, over time, for increasing inclusion of the child's and adolescent's opinion in medical decision-making in clinical practice and research (Katz et al. 2016).

A paediatric patient or a minor can be defined as a patient who has not reached the legal age of majority (in most countries, 18 years of age), a patient younger than 18 years. An adolescent refers to a person in the transition between childhood and adulthood, classically defined as 13–18 years of age. A child refers to a person from the ages of 1 through 12 years, and an infant refers to a person in the first year of life (Katz et al. 2016).

Children and parents have the right to informed participation in all decisions involving their health care so that they can make informed consent. Participation in decision-making requires advance information about all measures that need to be taken. The right of children to participate in their health care requires that staff members shall create an environment based on trust. Staff members shall have the capacity to listen, share information and give sound guidance. They have to respect the right of children to express their view

in all matters affecting them, give due weight to their opinion in accordance with their competence and render a culturally appropriate interpretation of the child's view and accept that children have the right to not express an opinion or to express their views through their parents (European Association for Children in Hospital 2016).

EACH Charter points out that the rights of the children and parents to informed consent require that staff members respect the child's and the parents' ability and competence. The staff need to provide adequate and timely information to the child and the parents regarding their child's health condition, the purpose and value of treatment, the process and the risks. They have to offer adequate, reliable information on alternative forms of treatment. They have to advise and support the child and the parents to evaluate the proposed course of action and acknowledge and take seriously the child's and parents' knowledge and experience relating to their child's general health condition or present condition (European Association for Children in Hospital 2016).

Children have the right to express their views and may disagree with their parents. Providing they are mature enough to make decisions in their own best interests, staff should respect the child's opinion, depending on the stipulations of national laws. Staffs are required to proceed with the utmost care to properly evaluate the situation. Hospital staff should also ensure that the necessary counselling and support is given to the parents (European Association for Children in Hospital 2016).

4.4 Role of Risk Assessment and Co-morbidity Scores

Transplantation carries a significant risk of morbidity and mortality, and these should be considered regarding the 'need' to transplant, based upon risk of disease, versus risk of the transplant; often this can be finely balanced. Suitability must be individualised to each patient need and requirements and discussed in detail with the patient with regard to the decisions.

Some patients are not solely living with the haematological disease or disorder and may have other factors that need to be taken into account. The presence of one or more diseases or disorders along with a primary diagnosis is called co-morbidity. This may be psychological or physical and may include illnesses such as diabetes and cardiac, respiratory or renal disease. Sometimes social and practical considerations may exclude a patient from undergoing stem cell transplant, yet as nurses we must aim to support where possible to ensure the best treatment options can be delivered.

Co-morbidity index tools have been used to predict outcomes in patients with cancer for several years, and some validated index tools such as Charlson co-morbidity index (CCI) consider medical history to estimate a prognosis or one-year mortality. Each factor is assigned to a point number of 1, 2, 3 or 6. Patients may have more than one disorder in each group, clearly increasing risk; however, the CCI was felt not necessarily relevant to patients undergoing HSCT because the factors within the groups would often already be considered an exclusion to transplant and did not reflect frequent morbidities experienced by haematology patients (Sorror et al. 2005). Subsequently the HCTI, which is considered more relevant to HSCT, was designed. This tool reflects the conditions that some of the patients face prior to transplant, which may be as a result of previous therapies used to treat the disease or indeed the disease itself and can be used to risk assess potential co-morbidity prior to allogeneic transplant.

Karnofsky Performance Status, also known as KPS, has scores ranging from 0 to 100 (0 being deceased and 100 being normal with no problems with activities of living or disease present).

KPS can be used to infer a patient prognosis and ability to perform activities of normal living. Dependent on the indication for transplant and patient wellbeing prior to commencing condi-

tioning, a KPS may limit options and be suggestive of outcome (Karnofsky et al. 1948).

100	Normal; no complaints; no evidence of disease
90	Able to carry on normal activity; minor signs or symptoms of disease
80	Normal activity with effort; some signs or symptoms of disease
70	Cares for self; unable to carry on normal activity or to do active work
60	Requires occasional assistance, but is able to care for most of their personal needs
50	Requires considerable assistance and frequent medical care
40	Disabled; requires special care and assistance
30	Severely disabled; hospital admission is indicated although death not imminent
20	Very sick; hospital admission necessary; active supportive treatment necessary
10	Moribund; fatal processes progressing rapidly
0	Dead

Post-transplant performance scores can be used to determine ongoing treatment. Similar to the KPS, the Lansky score is specific to children and activities that they will encounter (Lansky et al. 1987) and may be the preferred tool in the paediatric setting.

100	Fully active, normal
90	Minor restrictions in strenuous physical activity
80	Active, but gets tired more quickly
70	Greater restriction of play *and* less time spent in play activity
60	Up and around, but active play minimal; keeps busy by being involved in quieter activities
50	Lying around much of the day, but gets dressed; no active playing participates in all quiet play and activities
40	Mainly in bed; participates in quiet activities
30	Bedbound; needing assistance even for quiet play
20	Sleeping often; play entirely limited to very passive activities
10	Doesn't play; does not get out of bed
0	Unresponsive

4.5 Fertility Preservation

With advancing treatments more and more women and children are cured of a cancer or haematological disease but may subsequently be deprived of their ovarian function or exposed to premature menopause due to the ovarian toxicity of treatments. Any patient undergoing therapy likely to impair fertility should be referred according to local referral pathway.

Fertility is a well-known and significant concern for patients receiving high-dose chemotherapy +/− radiotherapy. However, the risk to fertility depends on the treatment received and the age of the individual at transplant. Evidence suggests that some young patients under the age of 16 at transplant may recover some gonadal function in later life (Suhag et al. 2015); however, this is dependent upon conditioning therapy, although the majority of the patients treated will be rendered infertile as a consequence of treatment. In male patients, there is some evidence that following induction therapy spermatogenesis may recover after 5–10 years of treatment, but this is very much variable (Tal et al. 2000, Viviani et al. 1999). Azoospermia rates range from 10% to 70% in males following stem cell transplant; again, this is often dependent on conditioning agents employed (Anserini et al. 2002, Jacob et al. 1998).

Fertility options must be discussed prior to initiation of ANY chemotherapy regime, and consequently many patients should have already had a discussion regarding fertility preservation well before transplant discussions are undertaken particularly if they have had induction therapy for their diagnosis. However, it is also essential for this to be clarified and discussed in detail prior to transplant conditioning.

Although ovarian function is more affected by chemotherapy and certainly high-dose regimes, female fertility preservation remains challenging. Egg harvests are not often viable for later fertilisation. IVF followed by embryo storage can be more effective but takes 2–3 weeks revolving

around the menstrual cycle and is not always feasible, especially in newly diagnosed patients with aggressive disease. Post-transplant, donor eggs may be a possibility for some women who may have limited options and should be explored in a full discussion with a fertility specialist.

Male patients should be offered sperm storage before initiation of any treatment. Radiotherapy and Alkylating agents amongst others have a severe impact on spermatozoa. Assuming that masturbation is possible, this is much simpler to organise than for female patients. It can usually be arranged and performed quickly in an andrology department. Once collected, the semen is analysed for sperm number, motility and quality. Quality of the sperm may be affected by several factors, including disease and current wellbeing of the patient.

4.6 Fertility Preservation in the Paediatric Population

The numbers of long-term survivors following haematopoietic stem cell transplantation (HSCT) have been noticeably increasing in recent years. Preparative regimens are associated with a high risk of infertility. Infertility is considered a major late effect in patients receiving haematopoietic stem cell transplantation (HSCT) (Borgmann-Staudt et al. 2012).

The infertility induced by cytostatic drugs is dependent on type and dosage of the drug used and also on the patients' age at the time of treatment.

More than two-thirds of former paediatric patients who had received allogeneic HSCT showed signs of impaired fertility. Significant risk factors were total body irradiation (TBI) for males and busulfan (Bu) for females (Borgmann-Staudt et al. 2012).

For radiation therapy, variables for infertility risk also include the:

- Age and developmental maturity of the patient
- Dose and fractionation of therapy
- Site of radiation therapy

The oocyte median lethal dose for radiation therapy is less than 2 Gy and sperm production is susceptible to damage at doses of more than 1.2 Gy; testicular Leydig cell function seems to be present at radiation doses up to 20 Gy (Fallat et al. 2008).

The alkylating agents, such as cyclophosphamide and busulfan, which have frequently been used in the treatment of childhood cancer, are far more gonadotoxic than other chemotherapeutic agents (Schmidt et al. 2010).

Hypogonadism is common after HCT (Sklar et al. 2001; Smith et al. 2014). In both boys and girls, hypergonadotropic hypogonadism (primary gonadal failure) is more common than hypogonadotropic hypogonadism (due to hypothalamic pituitary dysfunction) (Baker et al. 2009).

Children with hypogonadotropic hypogonadism have an absence of sex hormone production, delayed puberty, delayed pubertal growth spurt and a decrease in final adult height (Bourguignon 1988).

The type of presentation depends on the pubertal status at the time of HCT (Dvorak et al. 2011; Sanders et al. 2011). Puberty status is defined in two categories: 'Pre-puberty' for children aged up to 12 years and 'puberty' for children aged 13 years and older at the time of HSCT (Borgmann et al. 2011).

The earliest manifestation of impaired sex hormone production is delayed puberty in prepubertal patients, but older patients may show asynchronous or incomplete pubertal development, primary or secondary amenorrhea and infertility due to azoospermia or premature menopause. Sex steroids are also required for the growth spurt during adolescence. Delayed or incomplete puberty occurs in about 57% of females and 53% of males (Dvorak et al. 2011; Sanders et al. 2011).

In prepubertal males, the only option here is testicular tissue freezing. Options for use are autologous transplantation, xenografting or in vitro maturation. No children have been born from the use of prepubertal test tissue. In post-pubertal males, the most common option here is freezing of ejaculated sperm, but storage of testicular tissue is also a possibility (Shenfield et al. 2004).

4.6.1 Fertility Counselling

Studies emphasise the need for comprehensive counselling for patients undergoing HSCT, particularly those receiving TBI- or busulfan-based preparative regimens and their parents regarding fertility-preserving measures (Borgmann-Staudt et al. 2012).

Counselling patients of child-bearing age or their parents regarding future fertility when faced with a life-threatening cancer diagnosis is difficult but extremely important. Therefore, the health-care team has a responsibility to provide screening to identify these patients, provide education so that an informed decision can be made as rapidly as possible and have a team ready to preserve fertility once a decision has been made.

4.6.2 When?

Counselling at the primary diagnosis would be ideal.

In the current treatment era, optimal care for paediatric patients with cancer would include fertility preservation options at diagnosis prior to therapeutic exposures that can cause azoospermia. Sperm banking can be offered to even early pubertal patients, while development of methods to preserve spermatogonia from prepubertal patients represents an area of active research (Dilley 2007).

4.6.3 Issues

Fertility preservation is often possible, but to preserve the full range of options, fertility preservation approaches should be discussed as early as possible, before treatment starts. The discussion can ultimately reduce distress and improve quality of life. The discussions should be documented in the medical record (Loren 2013).

In 2015, the *Nordic Network for Gonadal Preservation after Cancer Treatment in Children and Young Adults* revised its Recommendations on Fertility Preservation (RTP) for girls and young women with childhood cancer:

> 'All girls should be examined regarding pubertal development (Tanner stage and menstrual history) at diagnosis and should be informed of the risk for impaired fertility following the planned treatment'.

4.6.4 Who?

Regarding this, in 2013 the original language used by the American Society of Clinical Oncology (ASCO) has been revised: The word 'oncologist' was replaced with 'health-care provider' to include medical oncologists, radiation oncologists, gynaecologic oncologists, urologists, haematologists, paediatric oncologists and surgeons, as well as nurses, social workers, psychologists and other no physician providers.

Regarding the role of health-care providers in advising patients about fertility preservation options, ASCO recommends:

> All oncologic health care providers should be prepared to discuss infertility as a potential risk of therapy. This discussion should take place as soon as possible once a cancer diagnosis is made and before a treatment plan is formulated. (Loren et al. 2013 Recommendations for Fertility Preservation for Patients with Cancer).
>
> However, what remains unclear is how these discussions are initiated, whether these discussions occur with all patients and which members of the oncology team are responsible for communicating with patients about these risks and available options (Nobel Murray et al. 2015).

In 2008, the bioethics committee, 2006–2007, from the American Academy of Paediatrics (AAP) published in this technical report reviews the Guidance for Counselling of Parents and Patients about Preservation of Fertility Options in Children and Adolescents with Cancer.

'Evaluation of candidacy for fertility preservation should involve a team of specialists, including a paediatric oncologist and/or radiation oncologist, a fertility specialist, anesthetist, and a mental health professional.

1. Cryopreservation of sperm should be offered whenever possible to male patients or families of male adolescents.
2. Current fertility-preservation options for female children and adolescents should be considered experimental and are offered only in selected institutions in the setting of a research protocol
3. In considering actions to preserve a child's fertility, parents should consider a child's assent, the details of the procedure involved, and whether such procedures are of proven utility or experimental in nature.

   In some cases, after such consideration, acting to preserve a child's fertility may be appropriate.
4. Despite it's not an options for children, instructions concerning disposition of stored gametes, embryos, or gonadal tissue in the event of the patient's death, unavailability, or other contingency should be legally outlined and understood by all parties, including the patient if possible.
5. Concerns about the welfare of a resultant offspring with respect to future cancer risk should not be a cause for denying reproductive assistance to a patient' (Fallat et al. 2008).

However, in 2015, the Nordic Network and Nordic Society of Paediatric Haematology and Oncology (NOPHO) revised the recommendation provided in 2012.

4.6.5 Recommendations on Fertility Preservation for Girls and Young Women with Childhood Cancer

After treatment All girls who have received alkylating agents or abdominal irradiation should after sexual maturation be offered referral to a gynaecologist or fertility specialist for evaluation, counselling and considering the possibility for ovarian hyper-stimulation and cryopreservation of oocytes.

4.6.5.1 Menstruating Girls

If the girl is menstruating, mature enough to give informed consent and is facing cancer therapy with very high risk of infertility, therapy can be delayed 1–2 weeks, and ovarian hyper-stimulation and cryopreservation of oocytes may be considered. The responsible oncologist must be consulted to make sure that no contraindications, such as bleeding disorders or too long delay of cancer therapy, to such procedures are present. The girl should get information adjusted to her age.

4.6.5.2 All Girls Regardless of Maturational Stage

All efforts should be done to minimise the radiation exposure to the ovary, such as optimal dose planning and irradiation modality, shielding and oophoropexy. Present knowledge indicates that a radiation dose lower than 10 Gy may preserve some ovarian function.

Girls, who are facing or receiving oncological treatments associated with a very high risk of infertility, could be offered the experimental procedure of ovarian cortical tissue cryopreservation.

In menstruating girls, cryopreservation of ovarian tissue can precede controlled ovarian hyper-stimulation (see above). The responsible oncologist must be consulted to make sure that no contraindications to such procedures are present.

4.6.6 Recommendations on Fertility Preservation for Boys and Young Men with Childhood Cancer

4.6.6.1 Pubertal and Post-pubertal Males

All males who are physically mature enough to produce sperm should be offered cryopreserva-

tion of sperm before oncological treatment with potentially gonadotoxic effect (i.e. all chemotherapy and radiotherapy with the gonads in the radiation field) is started.

All boys should be examined regarding pubertal development (Tanner stage and testicular volume). If the volume of testes is between 6 and 8 ml, there is a reasonable probability of sperm in an ejaculate.

The boy should be informed by a professional, specially assigned for this purpose, e.g. an andrologist, paediatric endocrinologist or fertility specialist, according to local availability and routines. It is important that the autonomy of the boy is respected and that he is offered the opportunity of individual consultation.

If the boy is unable to produce an ejaculate, alternative methods like vibrator stimulation or electro stimulation during anaesthesia could be offered.

If the boy is unable to produce an ejaculate or has azoospermia, an invasive procedure to retrieve testicular sperm may be considered, provided that the boy is motivated himself. The responsible paediatric oncologist must first be consulted to make sure that no contraindications (such as risk of tumour spread (e.g. in ALL) or bleeding disorder) to such procedures are present.

The boy, as well as his parents, should get verbal and written information about the procedures and the legal implications. The information should be adjusted to the boy's age, and he must give his informed consent to the cryopreservation.

4.6.6.2 Prepubertal Boys

Boys, who are facing oncological treatments associated with a very high risk of infertility, could be offered the experimental procedure of testicular biopsy cryopreservation. At present, there are no methods to ensure fertility after such procedures; thus, further research is warranted. Since the patient number is limited, the cryopreservation and research should be centralised.

The parents and, if old enough, the boy should get verbal and written information about the research project and give informed consent to the cryopreservation and to participate in the research.

4.6.7 Techniques

The objective of ovarian tissues' cryopreservation is to maintain viability of tissue after long-term storage. It is the basis for all forms of fertility preservation for cancer sufferers. Cryopreservation requires cooling tissue from 37 °C to the temperature of liquid nitrogen (−196 °C), storing at this temperature and then rewarming to 37 °C at some later date.

Freezed ovarian cortex segments can be used for later thawing and transplanting either back to the ovarian site (orthotopically) or to some other location (heterotopically). The ovarian cortex is used because it is this part of the ovary that is particularly rich in primordial follicles. In order for cryoprotectants to penetrate the tissue, the cortical strips need to be no more than 2 mm thick. Tissue samples from cancer patients need to be evaluated by a pathologist to detect the presence of any metastatic cancer cells (Agarwal and Chang 2007).

Spermarche occurs over a wide age range and is associated with a highly variable testicular volume, including in individuals with testicular volumes of less than 5 mL, pubic hair stage I or both. As a result, intraoperative assessment of the biopsy sample at the time of tissue retrieval has been suggested to be useful for allocation of tissue to a specific freezing protocol (Anderson et al. 2015).

For pubertal patients in whom complete spermatogenesis has occurred, semen cryopreservation is a well-established option. Recommendations are that all men and teenage boys should be offered semen cryopreservation for prepubertal patients and pubertal patients who are not able to produce a semen sample; approaches for fertility preservation are experimental (Anderson et al. 2015).

Sperm cryopreservation after masturbation is the most established and effective method of fertility preservation in males. Sperm should be collected before initiation of cancer therapy because

of the risk that sperm DNA integrity or sample quality will be compromised.

Nevertheless, recent progress in andrology laboratories and with assisted reproductive techniques allows successful freezing and future use of a very limited amount of sperm; collection of semen through masturbation in adolescents may be compromised by embarrassment and issues of informed consent. Alternative methods of obtaining sperm besides masturbation include testicular aspiration or extraction, electro ejaculation under sedation or anaesthesia or from post masturbation urine sample. Testicular aspirates do not freeze well and cannot be used as a method of preserving sperm (Fallat et al. 2008).

4.6.8 Fertility Preservation Options for Children and Young Adults with Distinction Between Established and Experimental Options

- In prepubertal boys, before onset of spermatogenesis, testicular biopsy and cryopreservation are options (experimental). In pubertal and post-pubertal male patients, the ability to produce a sperm-containing ejaculate enables sperm cryopreservation (established); if this is not possible, testicular biopsy with cryopreservation of sperm or tissue is needed.
- In prepubertal girls, ovarian stimulation is inappropriate, so ovarian tissue cryopreservation can be offered (experimental). After puberty, cryopreservation is an option, but ovarian stimulation enables recovery of mature oocytes for cryopreservation or of embryos after fertilisation (established) (Anderson et al. 2015).
- *Safety of tissue with regard to contamination with tumour/leukaemia cells*. Cancer contamination in the cryopreserved tissue is a contraindication for re-transplantation. Experimental studies are ongoing regarding the in vitro maturation of oocytes for fertilisation from such tissue. Further research is warranted. The parents and, if old enough, the girl should get verbal and written information about the experimental procedure, its associated risks and legal implications and give informed consent to the cryopreservation (NOPHO).
- In the interest of the child, the PDWP recommends that counselling about fertility preservation (FP) opportunities should be offered to each patient receiving SCT, as part of the pre stem cell transplant (SCT) workup. The PDWP recommends that should be offered by a dedicated and trained task force that may include medical staff from the stem cell transplant unit as well as fertility preservation specialists. The presence of dedicated nurse staff and psychologists in the counselling task force should be considered to create a broader communication opportunity for the patient, who may be more at ease with non-medical staff (PDWP, EBMT 2017).

4.6.9 Sexuality in Adolescents and Young Adults

Children at risk for impaired growth as a result of cancer therapy should be examined regularly, with their growth plotted on the appropriate growth chart.

Monitoring should be more frequent from the time of expected onset of puberty through the fusion of growth plates at full sexual maturation (Nobel Murray 2015).

Although we know that, after the transplant, some adults process experience psychological and social issues, there is an absence in the literature about the ‘adolescents and young adult’ (AYA) HCT population (Cooke et al. 2011).

The AYA cancer population is a vulnerable group due to variety of social, psychological and developmental reasons. AYA patients also can have disturbed endocrine function, body image disruptions and sexual problems (Cooke et al. 2011).

Who should be in charge of talking with children? It is impossible to consider parent–child interactions on the topic of fertility without framing the issue within the larger, complicated topic of parent–child discussions about sex, given that the two are inextricably linked. Discomfort in the

general area of discussing sexuality will impact the parental willingness and perception of competence in discussing fertility, especially at a moment of high stress (Clayman 2007). The growing literature on parent–child discussions of sex reflects the tendency of mothers to discuss this topic more frequently with their children, particularly daughters; even when both parents are involved, they are more likely to talk about sex with daughters rather than sons (Clayman 2007).

In 2006, Sloper's study concludes that there was an emphasis on the need for professionals to raise the subject sooner, more frequently, in a low-key way and without ambiguity. Respondents wished professionals would treat them as partners, therefore prioritising their input over their parents.

4.6.10 Conclusion

Dealing with fertility preservation upon diagnosis of cancer is challenging even for a young adult patient. This issue is even more complex for paediatric patients where decision-making generally falls to the parents but where high cancer survival rates increase the possibility of survivors needing to confront infertility later in life. Parents and adolescent patients report that achieving a healthy state is most important and that while they are interested in fertility preservation options, they may not be willing to delay treatment for pursuit of those options. Optimal care of paediatric cancer patients undergoing gonadotoxic therapy should include enrolment in available trials that will continue to refine knowledge of the effects of therapy on fertility for both male and female patients. Patients and families need information at diagnosis regarding the potential impact of therapy on fertility as well as referral to appropriate specialists for fertility preservation when desired. Studies and resources that allow potentially fertility-sparing interventions such as ovarian cryopreservation will not only need to be expanded, but adequate education and support for oncology providers who screen for patients at risk will be key. For patients that did not undergo fertility-sparing procedures prior to treatment, careful monitoring of reproductive function is warranted, and current technologies will still allow many of those patients to parent their own biological children (Dilley 2007).

4.7 Transplant Workup

HSCT is often considered as part of a therapeutic pathway, dependent on disease response and initial presentation. It is often proposed as a consolidation treatment to avoid a relapse. Prior to discussions regarding transplantation, it must be considered that the recipient can withstand the procedure without excessive risk and that there is no contraindication and the disease status is suitable to undergo the procedure. Transplanting patients with relapsed or relapsing disease may not provide sufficient benefit for the patient given the risks of the procedure and is often considered as futile. Pre-transplant assessments (disease status, bloods with virology status, radiology, cardiac, pulmonary and renal examinations) must be undertaken, and the results of these along with suitable donor medical clearance and cell availability are essential to ascertain that transplant is a valid option.

The results of this pre-transplant assessment will help to inform and adapt the transplant modality: conditioning regimen, type of graft, stem cell source and post-transplant strategy (immunomodulation, DLI). It also allows doctors to detect any abnormalities that could lead to post-transplant complications. This complete review serves as a reference and facilitates comparison of results of the examinations carried out before and after the transplant. In some cases the pre-transplant workup/assessment may mean that the risk of transplant is considered too great and therefore is no longer a suitable option due to higher-than-acceptable rates of morbidity and mortality and should be discussed with the patient. The previously mentioned morbidity indexes are useful in helping to determine this.

During transplant workup, the patient should be offered to meet other members of the multidisciplinary team such as social worker, dietician,

physiotherapist, psychologist, etc. where possible.

Transplant workup may vary from centre to centre and will be dependent on clinical indication. The list below is not exclusive but gives indication of workup required prior to transplant admission. The transplant coordinator would usually organise and collate this information and results.

- Full blood count.
- U & E and liver function profile.
- Virology transplant assessment including HIV; Hep B, C, and E; CMV; and EBV status.
- Group and save sample.
- HLA antibody screen.
- Coagulation.
- Tissue typing and verification typing of patient and donor for allogeneic transplants.
- Patients who have been heavily transfused prior to transplant should have serum ferritin levels taken to identify iron overload, >1000 ng/ml.
- Cardiac function is assessed by echocardiography (ECHO) or MUGA scan (ECHO is favourable). Healthy individuals typically have left ventricle ejection fractions (LVEF) between 50% and 65%.
- Calculated creatinine clearance or eGFR to estimate renal function.
- Pulmonary function tests
- Bone marrow aspirate and trephine +/− cytogenetics, dependent on disease and cytogenetics at diagnosis.
- Lumbar puncture +/− IT chemotherapy if acute lymphoblastic leukaemia or CNS disease/other clinical indication.
- CT/PET scan for lymphoma patients and other clinically indicated patient group.
- Double lumen central venous catheter.
- ECG – a 12-lead electrocardiograph.

Sufficient cell collections are required with a minimum PBSC (HPC-A) of 2×10^6/kg $CD34^+$ or BM (HPC-M) of 2.0×10^8/Kg MNC cells for infusion unless instructed otherwise by the transplant consultant for autologous transplantation and PBSC (HPC-A) of 4×10^6/kg $CD34^+$ or BM (HPC-M) of 4.0×10^8/Kg for donor harvested cell infusion. Donor cell collection results are not normally known prior to admission as the donor cells are not often cryopreserved and are coordinated a day prior to infusion (local policy may differ slightly), but clearance and agreement of the donor must be confirmed prior to patient admission.

4.8 Venous Access Devices: Principles of Placement and Care

Since the introduction of vascular access devices (VAD) in the seventeenth century and the first intravenous (IV) infusion procedures during the cholera epidemic in 1832 (Rivera et al. 2005), IV therapy is slowly developing towards a part of the treatment that all haematology patients will experience. In most countries infusion therapy is underestimated with a high incidence of complications. Although the positive effect of an infusion team is well proven (Brunelle 2003; Rutledge and Orr 2005), IV therapy still is a major burden for most patients. Health-care workers still miss the state-of-the-art knowledge and skills to make the right choice for the right patients and to use the VAD as it should. For venous access, we now have several VAD options to choose from. The most recent overview of VAD shows all options available now (Chopra et al. 2013) (Fig. 4.1).

In many centres the first option for vascular access is inserting a peripheral intravenous cannula (PIVC) for the initial IV therapy. If inserted by experienced health professionals in the right vein for the right indication, a PIVC is often the first VAD the patient is offered. Unfortunately PIVC's are still used for irritating infuses for as long as veins are accessible. Even small veins at the back of the hands, wrists and the ante cubital veins are used even if this is restricting the patient

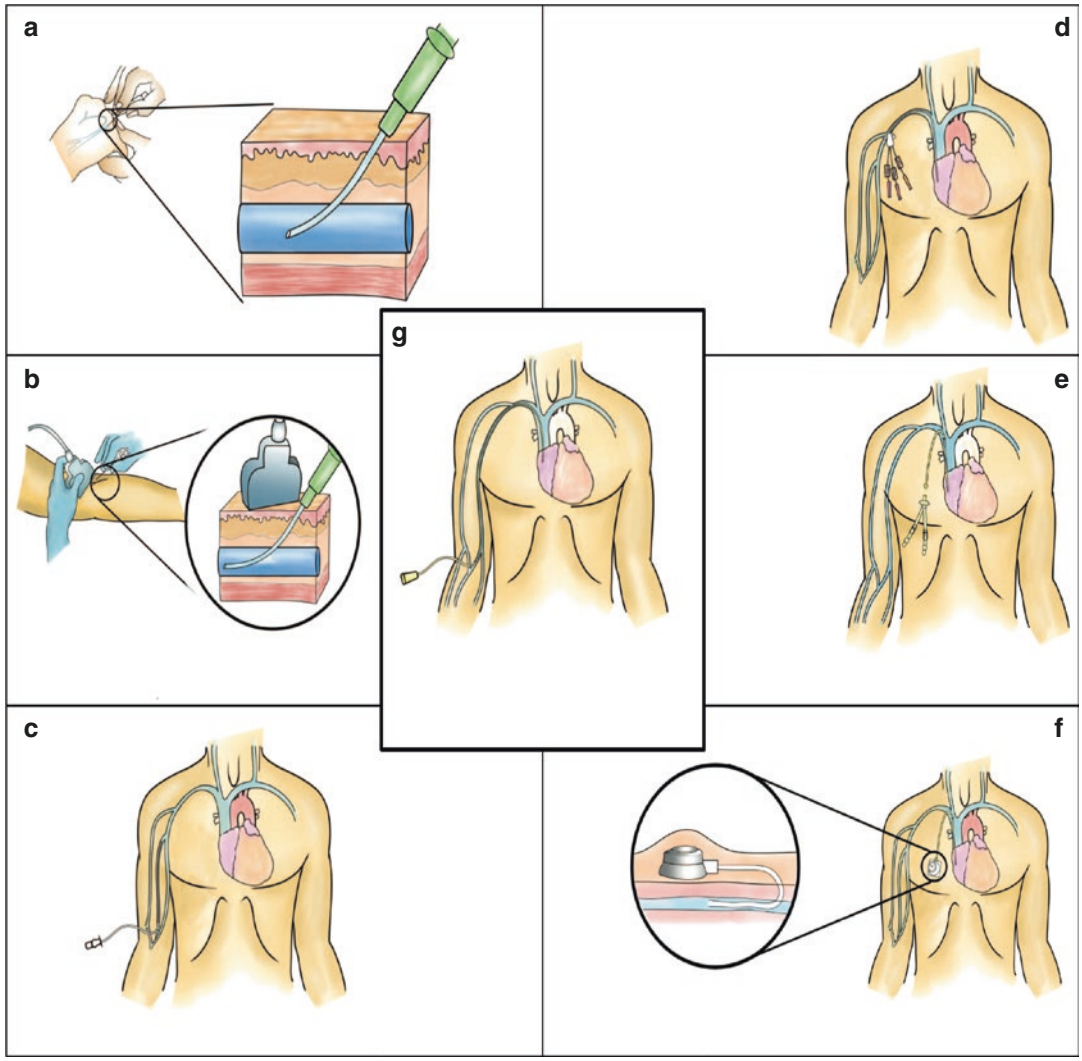

Fig. 4.1 Types of vascular access devices. (**a**) Peripheral IV catheter. (**b**) US-guided peripheral IV catheter. (**c**) Midline catheter, (**d**) Nontunneled central venous catheter. (**e**) Tunneled central venous catheter. (**f**) Implanted port. (**g**) Peripherally inserted central catheter

in mobility of hands and arms and often causing chemical phlebitis. Once peripheral veins are no longer accessible with conventional techniques and several hospital 'experts' accessed the last veins, an alternative is found in a tunnelled subclavian or jugular central venous access device (CVAD), mainly the so-called Broviac and Hickman catheters, named after the inventors of these VADs. A venous access port (VAP) is hardly seen in haematology treatment. The more invasive procedure for subcutaneous implantation of these VADs and the high risk during explanting of this type of VAD, these risks make the VAP in haematology not a real option.

During the EBMT congresses, the attention for vascular access is mainly limited to care and maintenance of CVADs in the annual nurses' group congress program. It is suggested that vascular access gets more attention in the EBMT program both for doctors and nurses and a multidisciplinary approach should be chosen. Vascular access should not be limited to care and

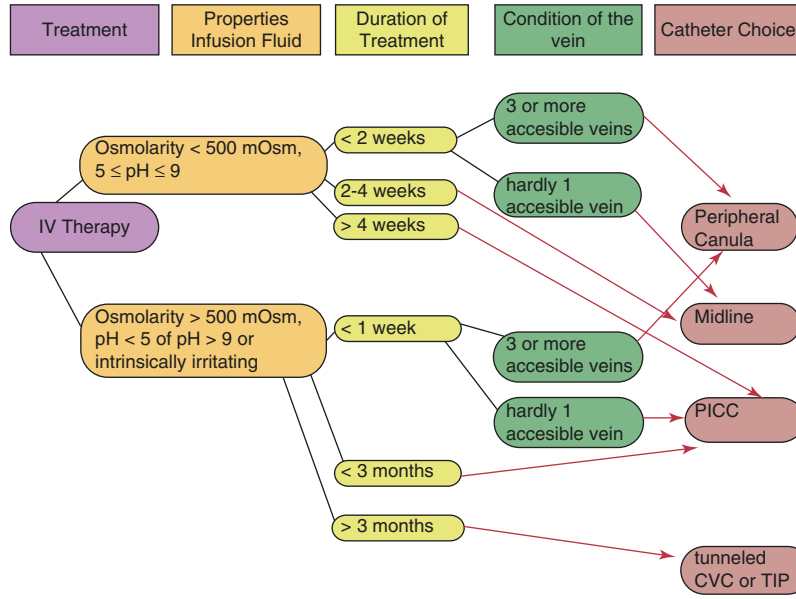

Fig. 4.2 Algorithm intravenous access for non-acute treatment in adults, University Medical Center Utrecht, 2008

maintenance after insertion of the VAD but should be focused on wellbeing and patient safety. An algorithm for choosing the right VAD for the right patient should start with the diagnosis and treatment plan. The best VAD should be chosen based on the pH and osmolarity of the drugs used during the whole treatment period and the vein condition and should include the option for (partial) home infusion treatment. In 2008 a model was introduced for non-acute patients VAD choice in the UMC Utrecht, the Netherlands (Giesen et al. 2008) (Fig. 4.2).

Extensive expertise, best materials, equipment and skills are needed to offer state-of-the-art insertion of the preferred VAD. The *Infusion Therapy Standards of Practice* suggests establishing or maintaining an infusion team for peripheral and central venous access device (CVAD) insertion, management and removal (Gorski et al. 2016). This chapter will mainly focus on insertion and care for VADs used in haematology patients. Based on haematology patient characteristics, only the tunnelled CVAD such as centrally inserted central catheters (CICCs) and peripherally inserted central catheters (PICCs) will be addressed.

4.8.1 Vascular Access Devices

Access to the venous system is required for all haematology patients. Access can be limited to drawing blood for research and diagnostic purposes and/or for administration of fluids, drugs and blood components. For drawing blood by venipuncture, a steel needle is used that will be removed immediately after the blood samples are collected using a vacuum collecting system.

For IV therapy, there are two options that can be used. Option one is a PIVC (Fig. 4.1a): a short flexible catheter that ends in a peripheral vein with limited blood flow. As seen in Fig. 4.1, a PIVC should only be used for non-vesicant drugs with an osmolarity <600 mOsm/L for a short period of time. An alternative PIVC might be a midline catheter. This VAD is inserted in the upper arm and the tip lies in the cephalic, brachial or basilic vein.

Option two is a CVAD with the tip of the catheter ending in a central vein with high blood flow. The definition for all CVADs is that the distal tip ends in a large vein close to the heart, the superior vena cava (SVC) or inferior vena cava (IVC) for femoral catheters. In adults, both SVC and IVC

have a blood flow up to 2–2.5 litre per minute and dilution of drugs happens so fast that the endothelium is not damaged.

Within the range of CVAD, a PICC (Fig. 4.1g) is seen more frequently in haematology patients, often as an alternative for a tunnelled CICC such as a Hickman catheter.

The insertion of a PICC is safe and non-invasive and can be performed even with low platelet counts. The PICC is first described in 1975 by Hoshal (1975) and has evolved to a VAD that can be the first option if central venous access in haematology patients is needed. A PICC can be used as an alternative to subclavian, internal jugular or femoral venous catheters. CICCs such as subclavian or internal jugular catheters may cause a pneumothorax, and femoral catheters are relatively more prone to infections. PICCs do not have these disadvantages.

A recent published algorithm in the MAGIC paper is based on latest evidence and supported by VA experts from many countries. This and other parts from this publication might also be helpful to use in your practice (Chopra et al. 2013) (Fig. 4.3).

Early studies show that a PICC is a safe and reliable option for central venous access (Maki et al. 2006; van Boxtel et al. 2008) (Table 4.1).

More recent results even come close to zero infections for PICCs if a bundle of preventive measures are taken (Harnage 2013). This bundle includes:

- Site selection
- Skin disinfection with 2% chlorhexidine in 70% gluconate
- Hand hygiene
- Maximum barrier precautions
- Daily control on indication
- Daily control on complications

Many clinicians still have the old-fashioned ideas that a PICC has a high incidence of infections and thrombosis, often based on their own

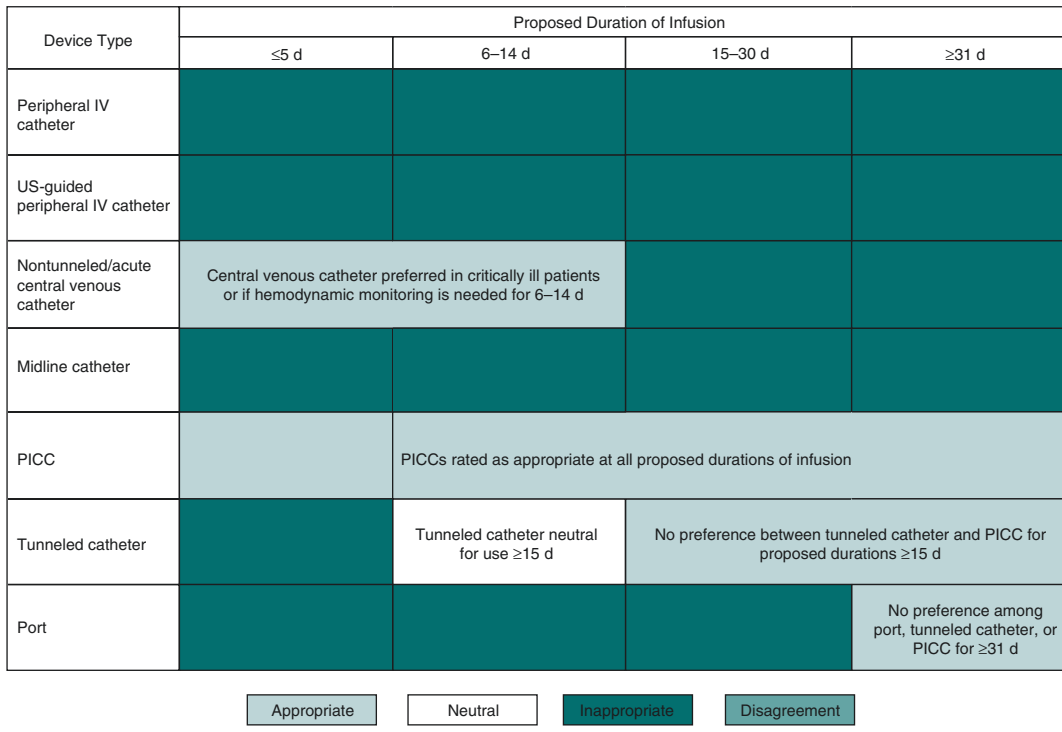

Fig. 4.3 Venous access device recommendations for infusion of non-peripherally compatible infuses

Table 4.1 CRBSI in PICCs

	No. of catheters	Catheter days	No. of BSI	CRBSI per 100 devices	CRBSI per 1000 cath. days
UMC inpatient	418	13.258	11	2.63	0.82
UMC outpatient	92	4397	1	1.09	0.23
UMC in- and outpatient	510	17.655	12	2.35	0.68
Maki inpatient	625	7137	35	2.4	2.1
Maki outpatient	2813	98.702	15	3.5	1.0
Maki in- and outpatient	3566		112	3.1	1.1

Table 4.2 Blood flow reduction based on vein diameter versus catheter size

Vein	Initial flow	2 Fr		4 Fr		6 Fr		8 Fr	
Cephalic (4 mm)	10	5	48%	3	28%	1.5	14%	0.5	0.5%
Brachial (5 mm)	25	13	53%	9	36%	6	22%	9	12%
Basilic (6 mm)	52	29	56%	21	41%	15	28%	9	18%
Axillary (8 mm)	164	100	61%	79	48%	62	38%	47	28%
Subclavian (10 mm)	400	256	64%	212	53%	175	44%	143	36%

experience with drum catheters and the Intra Cath. Since the introduction of ultrasound-guided PICC insertion around 2004 and the introduction of ECG tip confirmation techniques, only well-designed studies, later than 2005, should be analysed and used for local policies on VAD selection and insertion.

The correct position of a CVAD tip is at the lower third of the SVC (Gorski et al. 2016), cavo-atrial junction (CAJ) or right atrium (RA) (Espen 2009), lower third SVC or RA (RCN 2010), cavo-atrial region or RA (SIR 2010) and SVC adjacent to the RA (ASPEN 2010). A CVAD (PICC and CICC) can be used over a prolonged period of time, e.g. for multiple, extensive or long-term chemotherapy regiments, extended antibiotic therapy or prolonged total parenteral nutrition (TPN). The position of the catheter tip is very important in preventing thromboses. The distal tip of the CVAD should be placed at the junction between the superior vena cava and the right atrium to have the lowest incidence of thrombosis (Debourdeau et al. 2009). In a study from Cadman, CVADs with the tip in a distal position (lower third of the SVC or right atrium) had a 2.6% thrombosis. CVADs with tips in a proximal position were 16 times more likely to thrombose than those with the tip in a distal position. None of the 58 CVADs with the tip located in the right atrium thrombosed or caused complications (Cadman et al. 2004).

Another important criterion to prevent thrombosis is the vein-catheter ratio when choosing the catheter size. Based on the Nifong study, the catheter-vein ratio should be at least 1 to 3. For example, for a 4 French catheter, the diameter of the vein should have a minimal diameter of 4 mm. For a 5 French catheter, the diameter should be at least 5 mm, etc. (Nifong and McDevitt 2011) (Table 4.2).

Unfortunately many studies used for preparing guidelines and/or local policies for VAD selection are based on poorly designed retrospective studies. At the 2016 World Congress Vascular Access (WoCoVA), Pittiruti presented a thorough analysis of all published papers on catheter-related thrombosis (CRT). Relevant criteria, such as vein-catheter ratio and tip position, are often not taken as outcome criteria. In the review by Pilker et al., the authors included at least five studies dealing with PICCs inserted without US in their analysis for PICC-related thrombosis.

One of the studies used the same size of PICCs regardless of the vein's diameter. Only three of the studies had declared diagnostic criteria used for thrombosis. No study was prospective and/or randomised (Pikwer et al. 2012). The 'meta-analysis' from Chopra included any type of clinical papers (retrospective, non-randomised, etc.) and even abstracts and papers published on non-peer-reviewed journals. At least 14 of the 64 studies reported are old-fashioned with PICCs inserted without micro-introducer and without ultrasound, at the ante cubital fossa (Chopra et al. 2013). Fallouh and colleagues in their paper have not conducted any systematic assessment of the studies; they just discuss some studies from the literature (Fallouh et al. 2015). The review by Zochios is carried out without any systematic methodology. It describes a few studies about PICC-related thrombosis. Moreover, most of the studies quoted in his review are affected by bias related to the insertion technique, to the type of device used (inappropriate calibre) and to the retrospective design (Zochios 2015) (Fig. 4.4).

In those recent studies on haematology patients with a PICC, the CRT rate varies between 0 and 5.8%. If studies are well analysed, it is still evident that the expected rate of CRT with PICCs is not really different from the expected rate of CRT with CICCs. If an insertion bundle like the GAVeCeLT (Gruppo Aperto di Studio 'Gli Accessi Venosi Centrali) bundle for CRT prevention is implemented, the best options to prevent CRT are given:

1. Proper choice of the vein
2. Minimal trauma during venipuncture
3. Appropriate tip location
4. Proper securement

Bellesi 2013 (hemato-BMT)	5 %
Mitrovic 2014 (hemato)	3.8 %
Martella 2015 (hemato)	0 %
Sriskanadarajah 2015 (hemato)	5.8 %
Morano 2015 (hemato)	2.6 %

Fig. 4.4 Thrombosis rates in haematology patients with a PICC

Before starting the actual insertion procedure, the selected vein should be well examined, and the diameter of the vein should be documented.

As for all VAD insertion techniques, materials and procedures and care and maintenance are very important. To offer high-quality IV treatment and improve patient safety and satisfaction, insertion and the use of VADs should be limited to well-trained and certified health-care providers. Vascular access should be a specialty based on clear criteria-certified training programs and state-of-the-art materials and procedures (Moureau et al. 2013).

Although the insertion protocol might be slightly different in each country, a state-of-the-art protocol should be available and executed only by VA experts.

4.8.2 Care and Maintenance

If a CVAD is placed in the correct vein and the tip of the catheter is right position, the VAD should function properly with the lowest rate of complications possible. The care professional using the catheter should be sure that the catheter is fully functional before any drugs are administered. One has to be sure about functionality in order to take responsibility for any infusion. A back flash of blood is a good parameter, but not always possible with a poor tip position or minor thrombus at the catheter tip, allowing infusion but no aspiration of blood. If this problem is occurring since the CVAD insertion, it is most likely that the catheter is too short. If occurring after some time and normal functioning in the beginning, it might be a 'little' thrombus at the catheter tip. An x-ray of the chest might be part of the assessment. A urokinase or alteplase instillation in the catheter will help to restore patency if a thrombus at the tip is preventing aspiration of blood. The weekly care of the catheter and insertion site is different for a well-healed tunnelled CVAD with a subcutaneous cuff. This Hickman-type CVAD does not need a dressing covering the insertion site (Gorski et al. 2016). A PICC and other non-tunnelled CVADs need weekly dressing change. If sterile gauze is used in case of skin irritation or allergy, dressing change is every 2 days.

4.8.3 Flushing and Locking

Optimal functioning of a CVAD should be possible by using a strict flushing and locking protocol. In most protocols for preventing occlusion in CVADs, a heparin solution is still used. In a recent study in Leuven, Belgium, a randomised trial concluded that normal saline is a safe and effective locking solution in implantable ports if combined with a strict protocol for device insertion and maintenance (Goossens et al. 2013). This conclusion supports the hypothesis that a catheter lumen will not occlude if materials such as a neutral or positive displacement needle-free connectors are used and the technique of flushing and locking does not allow blood or any drug to stick to the catheter wall. Preventing any adhesion to the catheter wall also reduces the biofilm and bacteremia.

4.8.4 Securement

Use of tape or sutures is not effective for securement or VAD stabilisation. Suturing should be avoided to prevent needle stick injuries and infections. There are different types of securement devices. Frequently used is an adhesive attaching the catheter to the skin covered with a semipermeable folio. These securement devices should be changed together with the weekly dressing change. If dressing change is not well performed, there is a major risk of pistoning of the catheter increasing the risk of insertion site infections. A recently introduced subcutaneous securement device, an anchoring device, holds the catheter in place and stays in situ during dwell time of the catheter. This device is easy to remove after removal of the catheter by folding the base or with a firm pull of each part after cutting the base in two. The nitinol anchor pieces will stretch and not damage the skin or cause any pain. As for all insertion and care protocols, training is required for inserting and removal.

4.8.5 Occlusion

The care professional using the catheter should be sure that the catheter is fully functional before any drugs are administered. One has to be sure about functionality in order to take responsibility for any infusion. A back flash of blood is a good parameter, but not always possible with a poor tip position or minor thrombus at the catheter tip, allowing infusion but no aspiration of blood. If this problem is occurring since the CVAD insertion, it is most likely that the catheter is too short and aspiration is blocked when the opening of the CVAD is sucked against the vein wall. An x-ray should be made to confirm the diagnoses. If partial occlusion (easy infusion, but no blood return) occurs right after taking blood samples form the catheter lumen, it is most likely that the lumen is blocked by hemolyses of blood in the catheter or it might be a ‘little’ thrombus at the catheter tip. An x-ray of the chest might be part of the assessment. A urokinase or alteplase instillation in the catheter will help to restore patency if a thrombus at the tip is preventing aspiration of blood. CVADs should be regularly assessed for patency and proper function as defined by the ability to flush the catheter without resistance and the ability to yield a blood return. If the VAD is occluded, restoration should be done after assessment of the origin of dysfunction. If blood return is not possible from right after insertion, it might be that the catheter is too short.

The use of a thrombolytic agent such as urokinase can be used to restore patency. A 10,000ie vial should be diluted in 2 ml saline solution. The estimated volume of the catheter lumen should be instilled and left for 30–60 min before aspirating the solution. Slow infusion of 10,000ie urokinase can also be performed. Using this protocol is only on doctor’s order and dependent on the coagulation status of the patient.

For restoration of a totally blocked catheter lumen, a vacuum protocol can be used to restore patency. A three-way stopcock is placed directly at the blocked lumen. An empty 20 ml syringe is connected to one side. A 2 ml syringe with 10,000ie urokinase is connected to the other side. With the stopcock opened between the 2 ml syringe and the lumen, a firm vacuum is created. While vacuuming, the stopcock is switched to the urokinase catheter. Repeat this a second time. Leave this situation for 30–60 min and check

patency. If not successful, this procedure may be repeated once. In most cases the patency will be restored when done properly. If not, it might still have an effect after a few hours. This procedure should only be performed after training and doctor's order. It prevents removal of the CVAD and is a safe, cost-effective and patient-friendly method. If the origin of the occlusion is an acidic drug precipitate (low pH, less than 6), use a 0.1 N hydrochloric acid solution for declotting. For alkaline drug precipitate (pH greater than 7), sodium bicarbonate 8.4% or sodium hydroxide 0.1 mmol/L should be used. If the occlusion is from a lipid residue, 70% ethanol in a sufficient volume should been used to fill the catheter lumen; for paediatric patients, a dose of 0.55 mL/kg has been used with no more than 3 mL maximum. Use ethanol with caution with polyurethane CVADs as ethanol may damage the catheter material; refer to vascular access device (VAD) manufacturers' directions for use regarding exposure to any form of alcohol (Gorski et al. 2016).

4.8.6 CVAD Removal

If the indication for the VAD is no longer there or if the VAD is source of unsolvable complications, removal is indicated. Depending on the type of CVAD, removal can be done in the operating suite, bedside or at the patients home.

A venous access port (VAP) removal can only be performed as a sterile surgical procedure, mainly done in the operating suite. Also being an invasive procedure is the removal of a tunnelled, cuffed CVAD. A PICC however, even if the PICC is tunnelled, can be removed at the bedside or outside the hospital. After removing the dressing and the adhesive securement device, the PICC can easily be removed by gently pulling the catheter. After removal and checking on complete removal, there will not be much blood spilling, but compression of the insertion site is needed to prevent air embolism. The insertion site is covered with a dressing of sterile gauze or folio. If there is too much resistance at removal, it might help to apply warmth and try again after 10 min. If still not possible to remove the catheter, a specialised colleague should be consulted. If sepsis is suspected, the 'sterile' tip of the CVAD should be collected and sent for culturing.

If a PICC is removed at the end of indication without problems, the same site might be used for future access through the same vein. Thorough assessment, including scanning the route of the catheter, should be performed prior to insertion of the CVAD.

4.8.7 Pre-transplant Disease Assessment

Diagnosis and prognosis are based on the morphological examination of the blood and bone marrow blasts, the immunophenotype and the cytogenetic and molecular study (Willekens 2013).

Remission can be defined as the disappearance of clinical signs (anaemia, infections, bleeding, gingival hypertrophy, hepatomegaly, cutaneous leukaemia, etc.), but correction of cytopenias and disappearance of medullary blasts with a normal/normalising maturation of the bone marrow function should be observed. Moreover, recent and sophisticated methods (flow cytometry, molecular biology) can make it possible to follow the 'minimal residual disease' (MRD).

Diagnosis and remission can be determined by one or more of the following:

- Haematological status: review of the blood and bone marrow would indicate percentage of normal/abnormal cell population.
- Cytogenetics: karyotype becomes normal – cytogenetic abnormalities disappear (sensitivity: 1/100).
- Molecular: molecular biology (minimal residual disease) – undetectable transcript (sensitivity: 1/10000 to 1/100000).
- Imaging: CT/PET scan, MRI scan.
- Blood and urine tests (myeloma).

4.9 The Advocacy Role of HSCT Nurses

Patient preparation for HSCT involves the use of chemotherapy and/or radiotherapy to eradicate the underlying disease of the patient. This initial step leads to immunosuppression in order to trigger aplasia of the bone marrow and thus prevent graft rejection (Ortega 2004).

Throughout the procedure, the patient needs special care to overcome the complications associated with treatment. Nurses must be aware of the possible complications in order to play a role in preventing or early detection of alarming signs, such as sepsis, fluid overload and organ dysfunction, taking appropriate measures to minimise adverse effects and restoring the clinical balance of the patient. This care is very complex and requires a high level of skill to be able to provide those (Ortega et al. 2009).

Specific technical care activities require nursing knowledge and specific skills in the field of haematopoietic stem cell transplantation such as instrument manipulation, knowledge of technologies and use of special protocols to effectively intervene in complex situations that deal with acute complications (Dallaire 1999, 2008).

Nurses as 'health care provider' (Loren et al 2013) should be part of the interdisciplinary team The treatment team should be knowledgeable about fertility preservation so that they can educate patients and families about available fertility preservation options. It is important to consider and discuss all available fertility options with patients at the time of diagnosis (Fernbach et al. 2014).

Health-care providers should be prepared to discuss the negative impact of cancer therapy on reproductive health with their patients in the same way as any other risks of cancer treatment are discussed (Rodriguez-Wallberg and Oktay 2014).

Nurses provide a key role in patient education, providing pre- and post-transplant advocacy and counselling, planning hospitalisations and consultations and responding to patients' telephone calls. They also act as educators and role models to nursing students where appropriate and share knowledge and skills in accordance with local policies and JACIE guidelines. The presence of dedicated nurse staff and psychologists in the counselling task force is a mandatory.

Educating or teaching helps establish a relationship in order to encourage the individual to make free and informed choices. The nature of the disease and the transplant itself require patients to learn about it in order to cope with the consequences of treatment and to be involved in decision-making processes. Counselling and providing education is mandatory at each stage of the pathway.

Nurses should be able to work within a team, communicating with both the nursing colleagues and doctors, ensuring excellent medical care of the patient giving useful and clear information to the whole team. They help to identify early symptoms and are aware of the treatments to administer and the side effects to monitor and to accurately inform the medical teams of any changes or concerns.

Whatever the department or place of practice, the nurse's missions and activities are diverse and varied. Our primary task is the realisation of care intended to maintain or restore the health of the person.

4.10 Ethical Dilemmas

Ethics involves the meaning of words such as right, wrong, good, bad, ought and duty on a basis where people either individually or collectively decide that actions are right or wrong and whether one ought to do something or has a right to do something (Rumbold 1993).

In 1994, Tschudin states ethical dilemmas have become a major part of nursing with the ever more holistic and patient-centred care. Nurses are often drawn into case discussions, and their views are considered and valued. Medical ethics must allow access to care for all, without discrimination of any kind. Medical confidentiality or patient freedom is part of the rules of medical ethics.

Constant advances in haematology have raised challenging ethical dilemmas concerning end of

life, palliative care, patient information, donor concerns and impartiality and issues related to the risk we run to our patients.

In 2009, according to Langlois, ethical dilemmas often experienced by oncology and HCST nurses include:

- Therapeutic relentlessness – continuation of treatment, when the outcome is futile
- End-of-life intervention leading to death and euthanasia or cessation and withdrawal of treatment
- Transplantation in complex situation: refractory disease and older people

To cope with the therapeutic pathway of the patient, nurses must understand these complex situations. Regular staff meetings with a psychologist, palliative care unit and ethical committees and internal discussion in transplant ward will allow nurses to better understand this complex area by giving their nursing perspective to the team.

Ethical competencies in the transplant team allow us to solve new and unforeseen moral problems by knowing how to innovate in order to find the most legitimate and fairest behaviour possible in the face of a specific contextual situation.

The haematological pathway is often complex and uncertain. Treatments such as allogeneic HSCT can be associated with rapid changes in the care from curative to palliative (Howell 2010).

The resolution of an ethical dilemma for the nurse is related to the level of professional competence and understanding of the ethical concern allowing a better understanding of the context and of the complexity of the clinical situation. Ensuring that fully informed consent is provided by the patient is ethical dilemma which often occurs in medicine. Brykczynska (2000) identifies that the problem most often facing the haematology nurse regarding informed consent is not a lack of understanding as to what constitutes 'informed consent', or even how informed a patient needs to be for 'informed consent' to exist, but the vexed issue of conflict of interests.

Cancer invokes strong feelings and passions, and it is not infrequent to find a conflict of interest between members of the family, members of the health-care team and even members of the public as to whether to proceed with treatment or not. Emmanuel Kant's theory cited in Kemp Smith (1973) states that to act morally always treat other human beings as 'ends in themselves' and never merely as 'means'; by this Kant means that it is unethical to treat people as if they are objects. According to Kant it is fundamentally immoral to exploit a person without considering them an end in their own right. In transplantation where the side effects initially are extremely difficult and debilitating to the patient, it is sometimes difficult to justify such moral behaviour especially when nurses are striving not to inflict harm and to promote good.

What is often lacking, especially in nursing, is the courage and confidence to go through with a moral decision, which is basically an issue of personal moral development and personal integrity (Brykczynska 1997). It is the personal integrity of a particular nurse that will effect a change for the better or worse for an individual patient (Corner 1997).

4.11 Ethical Issues in Minors

Parents may act to preserve fertility of cancer patients who are minors if the child assents, and the intervention is likely to provide potential benefits to the child. Parents may act to preserve reproductive options of minor children undergoing gonadotoxic treatment as long as the minor assents, the intervention does not pose undue risk and the intervention offers a reasonable chance of net benefit to the child (Ethics Committee, ASRM).

When the child is immature, the decision to cryopreserve (or not) may be taken by the parents, unless it poses grave prejudice to the well-being/welfare of the child. The importance of preserving the possibility of having genetically related offspring in the future is generally recognised, and the parents will have to decide whether this benefit outweighs the current risk of intervention for their child.

Interdisciplinary consulting is mandatory; all specialties present in the caring team (oncologists, paediatricians, reproductive specialists, psychologists/counsellors) should be heard during decision-making about the best procedure. Experimental interventions in children can only be ethical if they can be considered to be therapeutic and in the best interests of the child. These considerations apply especially to development of techniques for prepubertal and peri-pubertal boys; although testicular tissue can be cryopreserved, how it should be used is not known at present (Anderson et al. 2015).

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