European Society for Blood and Marrow Transplantation

Nurses No Frontiers

Advanced Centre for Treatment, Research and Education in Cancer

National Conference on 'Hematopoietic Stem Cell Transplant Nursing'

December 14-15, 2018

Venue

Khanolkar Auditorium

Advanced Centre for Treatment, Research and Education in Cancer

Tata Memorial Centre Kharghar, Navi Mumbai

Organized by

Nursing Department, ACTREC

The TATA MEMORIAL HOSPITAL was initially commissioned by the Sir Dorabji Tata Trust on 28 February 1941 as a center with enduring value and a mission for concern for the Indian people. In 1952 the Indian Cancer Research Centre was established as a pioneer research institute for basic research - later called the Cancer Research Institute (CRI). In 1957 the Ministry of Health took over the Tata Memorial Hospital. The transfer of the administrative control of the Tata Memorial Centre (Tata Memorial Hospital & Cancer Research Institute) to the Department of Atomic Energy in 1962 was the next major milestone. The Tata Memorial Hospital and Cancer Research Institute merged as the two arms of the Tata Memorial Centre (TMC) in 1966 as a classic example of private philanthropy augmented by Government support with a mandate for Service, Education & Research in Cancer. Now under the umbrella of TMC ,six centres are spread over India.


Tata Memorial Hospital, Parel, Mumbai


ACTREC, Navi Mumbai


HBCHRC, Vizag

Homi Bhabha Cancer Institute
Sangrur, Punjab

BBCI Guwahati


HBCH Varanasi

INDEX

PROFESSOR & ANS, ACTREC
Dr. Meera S Achrekar

Greetings from ACTREC….

Ladies and Gentlemen

It gives me great pleasure to extend greetings and warm welcome to the faculty and delegates attending this conference hosted by nursing department ACTREC, in collaboration with EBMT and Nurses No Frontier group.

At this conference, let us celebrate our achievements and create our future vision in bringing out value addition to nursing service. This conference will provide a wonderful forum to refresh your knowledge and explore innovation in the field of nursing practice, patient education, and research. This conference will also provide opportunities for networking and exchanging ideas, on how to chart our journey forward to reach new heights

To put a conference of this magnitude together is not a small task. To that end, I want to thank our past and present Directors for their encouragement, Dr. Navin Khattry for wisdom and guidance, international and national speakers for accepting the invitation to be our faculty, my committee members for planning and logistic arrangements which was carried out with enthusiasm and the sponsoring organizations for their generous financial support. Last but not the least, I would like to thank all the delegates for their participation which is the foundation of this conference.

Have a productive and fun-filled time at this very special conference.

EBMT NG GEC CHAIR
Aleksandra Babic

Haematopoietic Stem Cell Transplantation (HSCT) is highly complex medical procedure and is in continuous evolution.

FACT-JACIE is a non-profit organization that certifies the adherence of transplant institutions to international quality standards and in many countries worldwide these accreditations are mandatory.

FACT-JACIE standards also requires that the Clinical Program has access to personnel who are formally trained, experienced and competent in the management of patients receiving cellular therapy.

Highly-complex nursing care is essential for treatment-related health problems within this setting of patients and early recognition of signs and symptoms and report to medical team is of utmost importance and might impact on patients and donor care.

EBMT Nurses Group Global Educational Committee (EBMT NG GEC) and Nurses No Frontiers Association (NNF) will be delivering the second blood and marrow transplantation (BMT) training course in ACTREC, Tata Memorial Center on December 14-15 2018.

During the training course, the participants will have the opportunity to network with their Indian and European colleagues and to discuss standards of BMT nursing care as well as novel treatments and the most frequent side effects.

Furthermore, a special overview of 1st level JACIE accreditation impact on patient care will be discussed.

I hope you will be enjoying the course and share your experience with your colleagues at your hospital.

DIRECTOR, ACTREC
Dr. Sudeep Gupta

“Nursing is a vital component of the modern practice of haematopoietic stem cell transplantation. This conference is timely and important for all institutions, departments, and nursing personnel who are engaged in this treatment modality.

I congratulate the organizers for assembling such distinguished individuals as faculty. I hope that the delegates will benefit from participation in the conference.”

DEPUTY DIRECTOR, CRC, ACTREC
Dr. Navin Khattry

I take this opportunity to welcome all the international and national faculty and delegates from all over the country. This event is the second nursing conference of our centre in collaboration with EBMT nursing group. After the success of the first meeting held in December 2016, we decided to conduct a second conference on practices of bone marrow transplant from nurses' perspective.

Nursing care forms the backbone of any bone marrow transplant unit, which directly impacts outcomes. Therefore it is imperative that our nurses learn the best practices in bone marrow transplantation from international and national experts. I am sure that deliberations from this two day conference will enable our nurses to improve care in their respective units and also standardise practices across the country. We are also helpful that a national nursing transplant group on the lines of EBMT nursing group is formed in our country too and I congratulate Dr Meera Achrekar for taking the first step in that direction.

I wish the organising team the very best for this meeting and wish the participants to have a joyful and fruitful time in the course of the 2 day meeting!

Program

DAY 1 Friday 14th December 2018		
08:00 - 08:30	**Welcome and Introduction**	Meera Achrekar Aleksandra Babic Navin Khattry Sudeep Gupta
Session 1 : Chairpersons – Sindhu Nair and Suman Kubal		
08:30 - 08:45	**Overview of JACIE process and implications for transplant program**	Aleksandra Babic
08:45 - 09:30	**Indications for HPC transplantation (autologous vs allogeneic)** • Standard indications – an update. • Experimental indications • High-dose preparative regimens (myeloablative, RIC, haplo)	Michelle Kenyon
09:30 - 10:15	**Care of immunocompromised patients** • Hematology/ oncology patient care (isolation and DPI) • Administration of preparative regimens, blood products, cellular therapy products, and other supportive therapies • HPC product infusion and patient management (cardiac dysfunction, neurologic toxicity, etc) • Recognition of cellular therapy complications and emergencies requiring rapid notification of the transplant team	Julia Ruiz, (ESP)
10.15 - 10.45 : BREAK		
Session 2: Chairpersons – Prathepa Jagdish and Shyla Sam		
10:45 - 11:30 1st part	**Early and acute complications in BMT setting, diagnosis and management** • Management of mucositis, nausea, vomiting and pain management • Central venous access devices (care of CVAD: Hickman, port and ICC) • neutropenic fever, management of thrombocytopenia and bleeding • Diagnosis and management of veno-occlusive disease of the liver • Respiratory infections • Fungal infections • Common viral complications • Multi-resistant bacteria – reducing the spread	Alberto Castagna Eugenia Trigoso
11:30 - 12:00	**Management of haemorrhagic cystitis**	Latha Gracelin P
12:00 - 12:45	**Supportive care of the HSCT recipient** • Principles of nutritional support • Psychological care: meeting information needs • Survivorship and quality of life • Palliative and end of life care: pain management	Marta Canesi
12.45 – 14.00 : LUNCH		

Session 3: Chairpersons – Kalaivani M and Anil James		
14.00 –14.30	Discharge instructions for BMT patients	Sherin Babu
14.30 -15.15	**Cell source and Apheresis** • HSC source, standard and new applications • Administration of growth factors for HPC mobilization and for post transplant hematopoietic cell reconstitution • HPC processing: principles of bone marrow harvest procedures and apheresis collection procedures • HPC cryopreservation • Extracorporeal photopheresis for GvHD	Aleksandra Babic
15.15 -16.00	**Graft versus Host Disease (GvHD)** • Acute vs chronic graft versus host disease: assessment criteria • Prophylaxis, treatment and care, supportive and complementary	Marta Canesi
16.00 - 16.30 : BREAK		
16.30 - 17.15	**ACTREC nurses clinical case presentation and discussion with all**	
DAY 2 Saturday, 15th December 2018		
Session 4: Chairpersons – Jessica Dsouza Rutuja Dandekar		
09:00 – 09:40	**Evaluation of post-transplant cellular therapy outcomes** • Diagnosis and management of HPC graft failure • Evaluation of late effects of allogeneic and autologous transplants, including cellular, pharmacologic, and radiation therapy.	Michelle Kenyon
09:40 – 10:30	**Identification, evaluation, and selection of HPC source, including use of donor registries** • Donor eligibility determination • Methodology and implications of human leukocyte antigen (HLA) typing. • Administration of ABO incompatible cellular therapy products and management of patients • Donor rights, confidentiality and privacy	Marta Cenesi Julia Ruiz-
10:30 – 11:00 : BREAK		
11:00 – 11:45	**Management of pediatric recipients** – clinical case presentations	Eugenia Trigoso
11:45 – 12:30	**Discussion with all on clinical cases presentation (different units)**	
12:30 – 14:00 : LUNCH		
Session 5: Chairpersons – Anita D'souza and Komal Mundhe		
14:00 14:30	**Quality indicators for BMT – 1st level JACIE accreditation**	Aleksandra Babic
14:30 – 15:15 **2nd part**	**Early and acute complications in BMT setting, diagnosis and management** • Management of mucositis, nausea, vomiting and pain management • Central venous access devices (care of CVAD: Hickman, port and PICC) • Neutropenic fever, management of thrombocytopenia and bleeding • Diagnosis and management of veno-occlusive disease of the liver • Respiratory infections • Fungal infections • Common viral complications • Multi-resistant bacteria – reducing the spread	Alberto Castagna Eugenia Trigoso
15:15 – 15:45	**Discussion with all on clinical cases of above complications**	
15:45 – 16:00	**Valedictory function**	

Aleksandra Babic is the Blood and Marrow Transplantation (BMT) Unit Coordinator and Quality Manager at the Oncology Institute of Southern Switzerland (IOSI) in Bellinzona, Switzerland. She previously worked as a Nurse Manager at the Mobilization and Apheresis Collection Facility at the European Institute of Oncology in Milan, Italy. Aleksandra's research interests focus on blood and marrow transplantation, apheresis and nurse education in developed and Low-and-Middle-Income Countries (LMIC). She is past-President of the European Society for Blood and Marrow Transplantation (EBMT) Nurses Group and a current chair of its Global Educational Committee. She is also a Board Member of the Nurses Group, holding a position of the Account Officer. Aleksandra is President of the non profit organisation Nurses No Frontiers (www.nursesnofrontiers.org) and a founder and past-President of the Italian Interdisciplinary Group in Cellular Therapy Manipulation and Apheresis (GIIMA, www.giima.eu)

Alberto Castagna is Paediatric Hemato-Oncology Nurse and is working in Paediatric Hematology, Oncology and HSCT Unit in Verona Italy, for the last eight years.
He is the Chair of Communication & Networking Committee for the Nurses Group of EBMT and a Board Member of Nurses No Frontiers with occupation as speaker during educational meetings and Information and technology manager.

Eugenia Trigoso has worked in the pediatric oncology and transplants units as the hospital universitari i politècnic la fe.
She is an active member of national and international nurses groups including, European group for blood and marrow transplantation (EBMT), the European oncology nursing society (EONS), the Spanish oncology nursing society and geet.
Eugenia is involved in several nurses training course in spain and abroad and has been a volunteer nurse at Barretstown, Ireland since 2009.

Julia Ruiz has been working as a RN in the Oncology and BMT Unit at Niño Jesus Childrens´ Hospital, since 1998. Currently she is the quality manager and data manager of the BMT Unit, Apheresis and Processing Unit since 2009, and actively participate in inspections as a JACIE Quality Manger Inspector. She is also a member of the Nurses Global Educational Committee and Spanish Nurses Group.

Latha Graceelin is a MSc Nurse , RN, Junior lecturer at the college of Nursing, Christian Medical College, Vellore, Tamil Nadu in the state of India. She is the Nurse Manager of the hemato-oncology ward of CMC, Vellore. She is an active participant and resource person in the hemato-oncology workshops and conferences.

Marta Canesi, an Italian Pediatric Hematology and BMT Unit staff nurse. She has completed her 1st level Master courses in Pediatric Nursing in 2010 and Intensive care nursing in 2013. She is graduated in MSN in Midwifery sciences in 2017. Marta is a member of an experts panel for the implementation of the gene therapy program to treat pediatric genetic diseases. In addition she is a nurse leader in Scientific Committee of the Children Global Medicine Program. Marta is an active member in Research Committee in EBMT Nurses Group (European Bone Marrow Transplantation) and Nursing Work Group of AIEOP (Italian Association of Pediatric Onco-Hematology. Besides this, she has numerous publications, posters and presentation.

Michelle Kenyon is a consultant nurse of BMT and her role spans the entire Blood and Marrow Transplant patient pathway and she has clinical and research interests in improving the patient experience from the start of their journey and supporting patients throughout their post-transplant recovery. Michelle is Secretary of the EBMT Nurses' Group, the nurse representative on the British Society of Blood and Marrow Transplantation Executive Committee, and Vice Chair of the EBMT UK NAP Group, a national group for UK nurses and allied health professionals. She has also authored The Seven Steps and The Next Steps, two patient information books, which are now used as the basis of informed consent for transplant recipients at many centers throughout the UK, and has co-edited the first EBMT Textbook for Nurses which was launched at EBMT 2018.

Sherin P Babu is a Bachelor in Nursing and working in RGCI&RC Delhi as a Charge nurse & Co-coordinator of haematology and BMT Nursing Department. He is officially posted as the trainer for the BMT nurses and given training to many nurses from various part of the country and also nurses from Sri-Lanka and Nepal. He plays an active role in research activities of Haematology unit of RGCI. Sherin is trained for USG Guided PICC LINE insertion.

Rosy Pinto, sister In-charge of BMT unit, ACTREC. She actively involves in patients (pre transplant, post transplant, during transplant). Currently she is an Executive Committee member of Oncology Nurses Association of India (ONAI). She has presented topics in national and international conferences and has presented poster in AONs conference in South Korea. She has few publications in ONAI journal.

Mumbai Sightseeing

Mumbai (formerly called Bombay) is a densely populated city on India's west coast. A major commercial hub, it is also India's largest city. On the Mumbai Harbour waterfront stands the iconic Gateway of India - a stone arch built in 1924 during the British Raj. Offshore, Elephanta Island holds ancient cave temples dedicated to the Hindu god Shiva.

Mumbai makes space for everyone and welcomes them with a warm heart. Mumbai is a city where tourists can enjoy a great nightlife. It is famous for its Juhu beach, other places of sightseeing like Gateway of India, Elephanta Caves, Prince of Wales Museum, Jehangir Art Gallery, Hanging Garden, Aquarium, Siddhivinayak Temple. Navi Mumbai too has attractions like the mini seashore, Wonders Park, Central Park, Utsav Chowk, etc.

Gateway of India

Elephanta caves

Marine Drive

CST Heritage building

Prince of Wales Museum

Chowpatty

Hanging Garden

Taraporewala Aquarium

Haji Ali

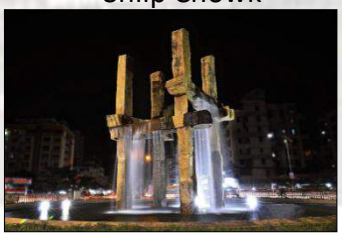
Siddhivinayak Temple

Bandra Sea Link

Mini Seashore

Utsav Chowk

Shilp Chowk



Central Park

Wonder Park

Overview of FACT/JACIE process and implications on BMT program

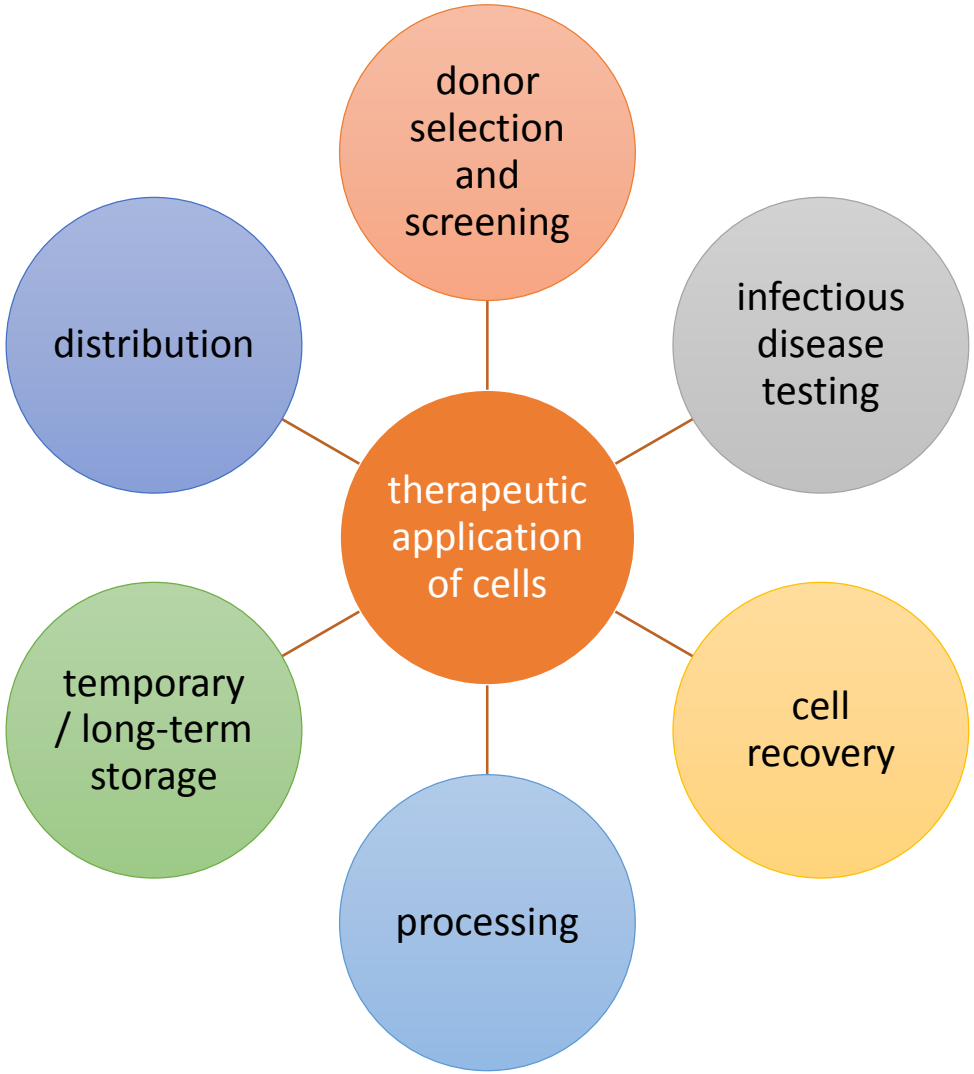
Aleksandra Babic

Oncology Institute of Southern Switzerland, IOSI – Bellinzona, CH

Nurses No Frontiers - Training course for HSCT nurses – India

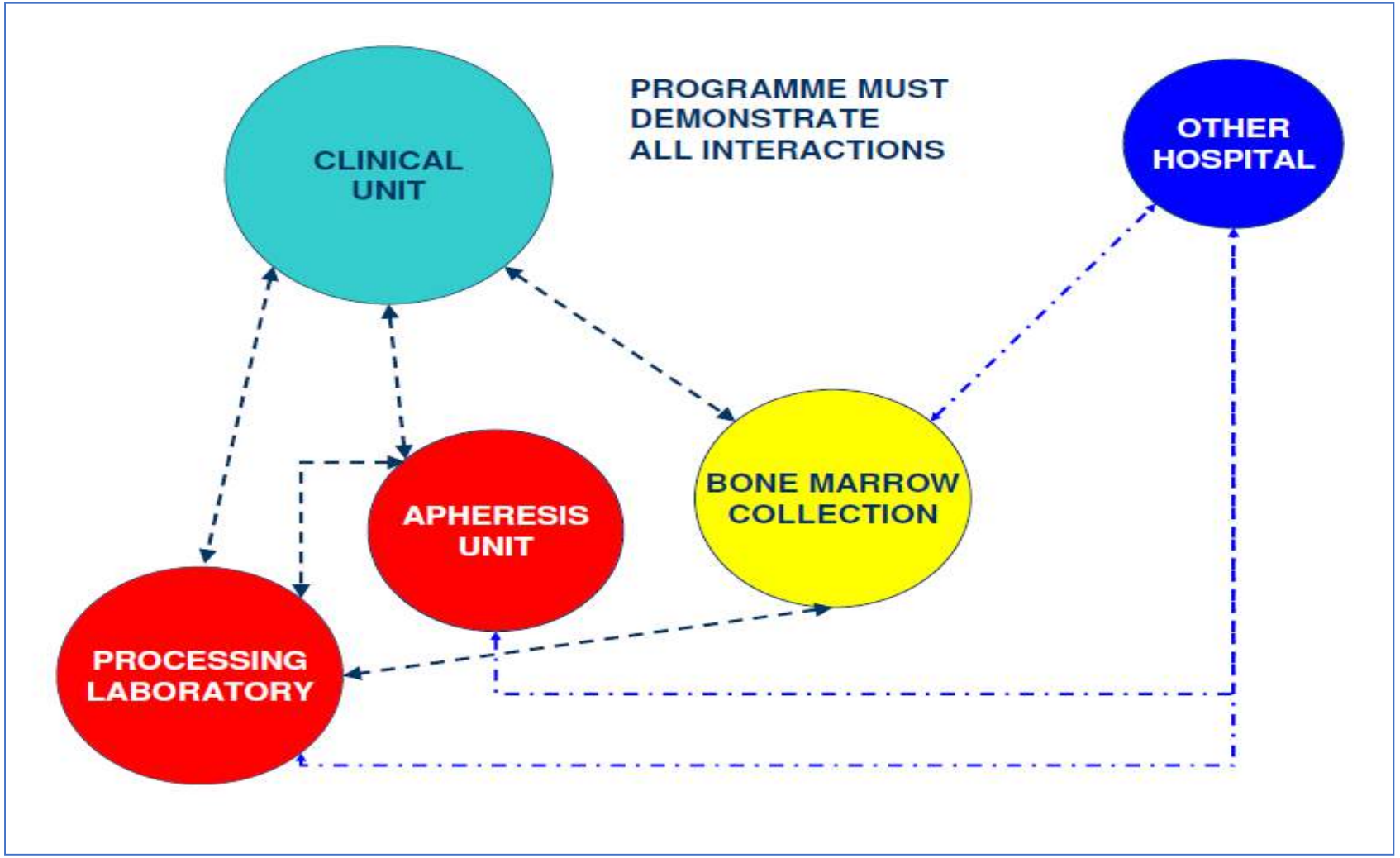
14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

HSCT is a complex process



Adapted from Tissue and Cell Processing: An Essential Guide. Edited by Deirdre Fehily, Scott A. Brubaker, John N. Kearney, and Lloyd Wolfinbarger. © 2012 Blackwell Publishing Ltd.

Interactions Between Services



8 most common problems in health care

1. Unknowing variation in clinical practice and service delivery
2. Errors of commission and omission
3. Waste
4. Failure to implement new knowledge and technology systematically and appropriately
5. Over-use and under-use – inappropriate care
6. Unsatisfactory patient experience
7. Poor quality clinical practice
8. Failure to manage uncertainty

New Taipei City, a Taiwan, ha causato 14 morti nel bilancio provvisorio dei media locali che annovera circa 20 feriti, di cui alcuni gravi.

(ansa)

Condividi

I vigili del fuoco hanno individuato il focolaio al settimo piano dove erano ricoverati 32 pazienti: l'allarme è scattato alle 4:36 (22:36 di domenica in Italia), mentre le fiamme sono state domate in un'ora con l'impiego di 76 mezzi e 208 pompieri. Le autorità locali hanno precisato che sono in corso indagini per far luce sull'incidente.

Ref. Ares(2014)20512

EUROPEAN COMMISSION
HEALTH AND CONSUMERS DIRECTORATE-GENERAL

Directorate D - Health systems and products

D4 – Substances of Human Origin and Tobacco Control

Brussel
SANCO. D4/ IH/ac ARES(201

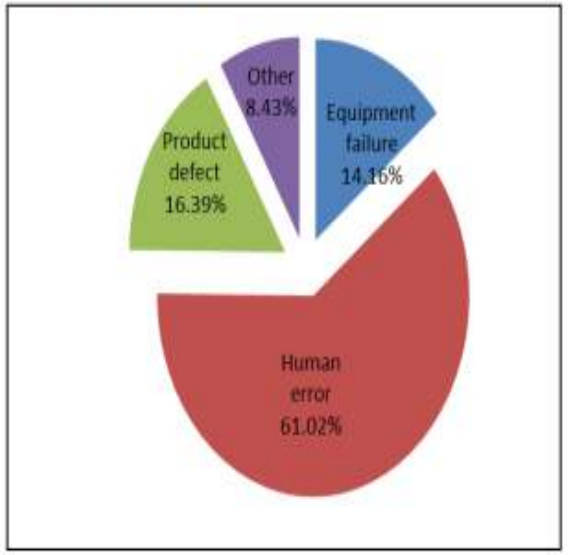
SUMMARY OF THE 2013 ANNUAL REPORTING OF SERIOUS ADVERSE EVENTS AND REACTIONS (SARE) FOR BLOOD AND BLOOD COMPONENTS (DATA COLLECTED FROM 01/01/2012 TO 31/12/2012)

2.4.3. Information by Specification of SAE

The 2,953 SAEs were attributed to one of the following specifications:

- **Human Error**: 1,802 SAE (61.02%)
- **Equipment failure**: 418 SAE (14.16%)
- **Product defect**: 484 SAE (16.39%)
- **Other:** 249 SAE (8.43%), including 'organisational errors' or unclassified SAE.

Figure 7: Serious adverse events per specification.



http://ec.europa.eu/health/blood_tissues_organs/docs/blood_sare_2013_en.pdf

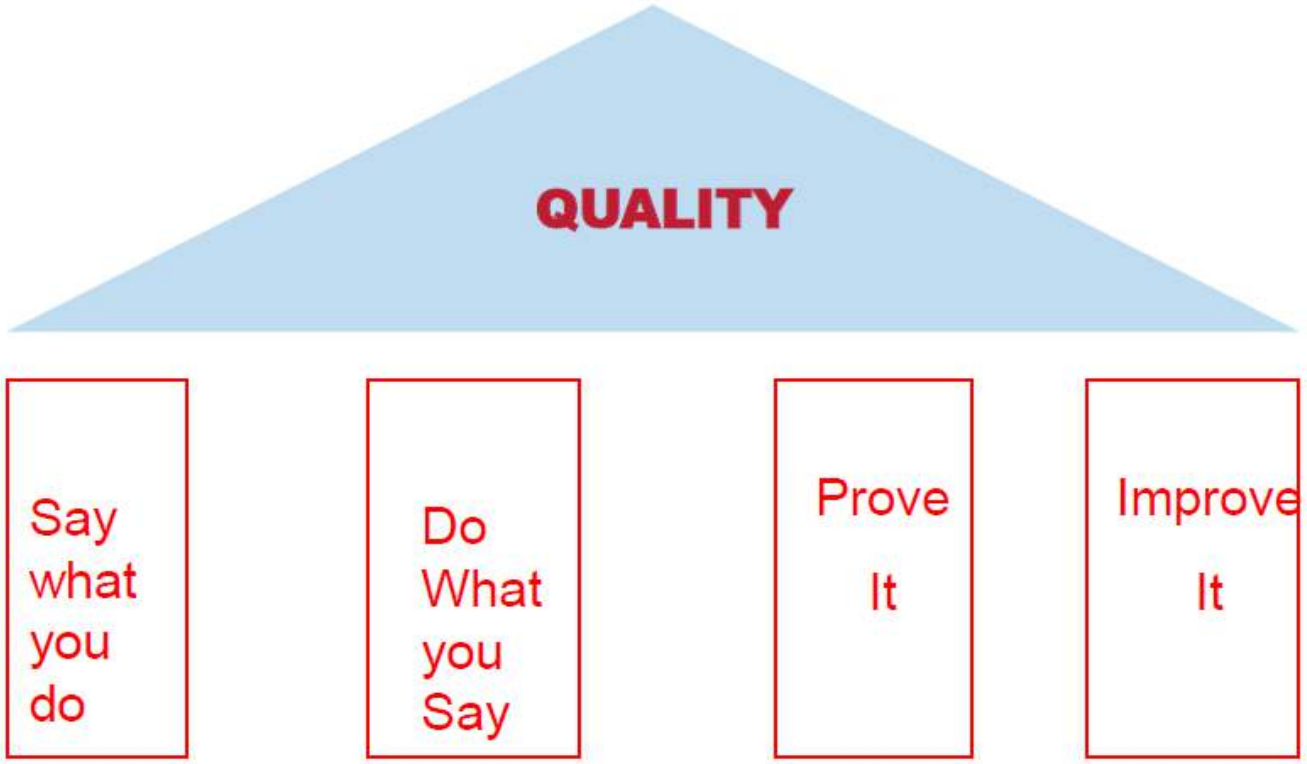
What is quality?

- Moullin (2002)
  - Quality leads to a service better meeting the patient's requirements, and increases patients confidence in the service; staff is more empowered and higher job satisfaction; better quality can reduce costs
- MacKenzie (2005)
  - Multidimensional & changeable concept
  - 'an acceptable compromise'
- Donabedian (2005)
  - reflection of values and goals current in healthcare and in the larger society

What is quality?

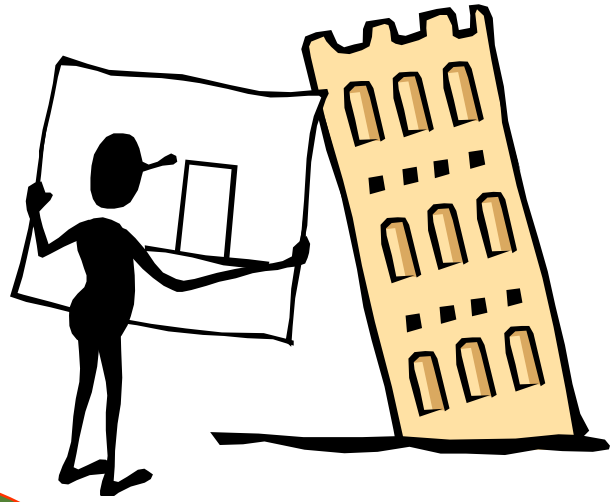
- US Institute of Medicine: Six dimensions of healthcare quality
  - Safe
  - Effective
  - Patient-centred
  - Timely
  - Efficient
  - Equitable

Pillars of quality



SOPS MEANS MORE SECURITY IN TERMS OF

VALIDATION

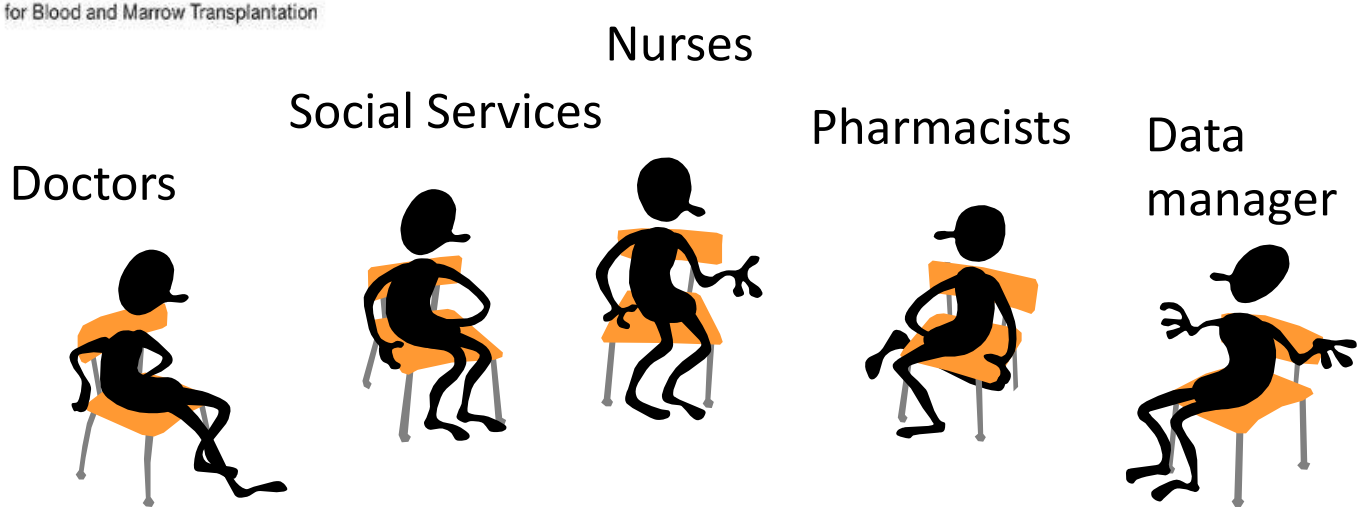


IMPROVEMENT

TRACEABILITY

MANAGEMENT OF DEVIANCE

COMUNICATION



TO OBTAIN A GOOD COMUNICATION INSIDE OF COLLECTION UNIT IS NECESSARY TO HAVE FORMAL MEETINGS AND TO RECORD THEM WITH AIM TO:

- **BETTER ORGANIZZATION**
- **INTERNAL AUDIT**
- **PROBLEM EVIDENCE**
- **FORMATIVE COURSES**

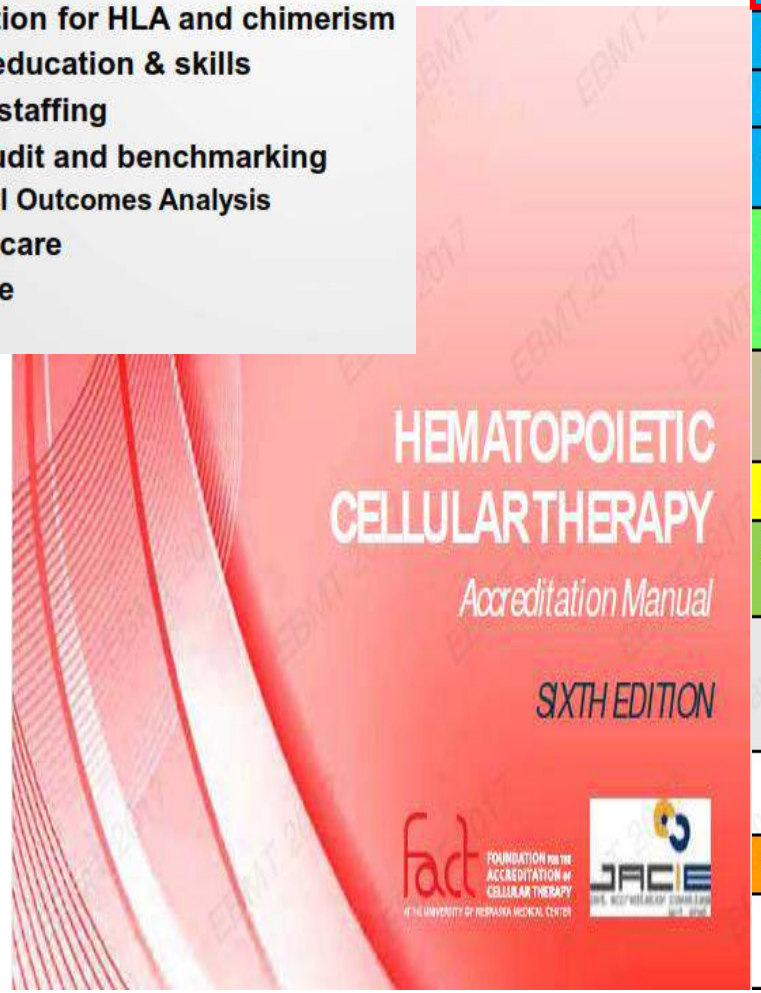
Healthcare accreditations

The International Society for Quality in Health Care

Accredited Organisations	Acronym	Country	Expires
Improvement of Quality and Care Security Department of Haute Autorité de Santé	DAQSS	France	September 2014
Taiwan Joint Commission on Hospital Accreditation	TJCHA	Taiwan	September 2014
The Council for Health Service Accreditation of Southern Africa	COHSASA	South Africa	January 2015
Danish Institute for Quality and Accreditation in Health Care	IKAS	Denmark	March 2015
Diagnostic Accreditation Programme, British Columbia	DAP BC	Canada	August 2015
Health and Disability Auditing Australia Pty Ltd	HDAA	Australia	August 2015
Joint Commission International	JCI	USA	August 2015
Malaysian Society for Quality in Health	MSQH	Malaysia	May 2016
Quality Improvement Council	QIC	Australia	May 2016
National Accreditation Board for Hospitals & Health Care Providers	NABH	India	August 2016
DAA Group Limited		New Zealand	November 2016
AABB	AABB	USA	December 2016
Netherlands Institute for Accreditation in Healthcare	NIAZ	Netherlands	January 2017

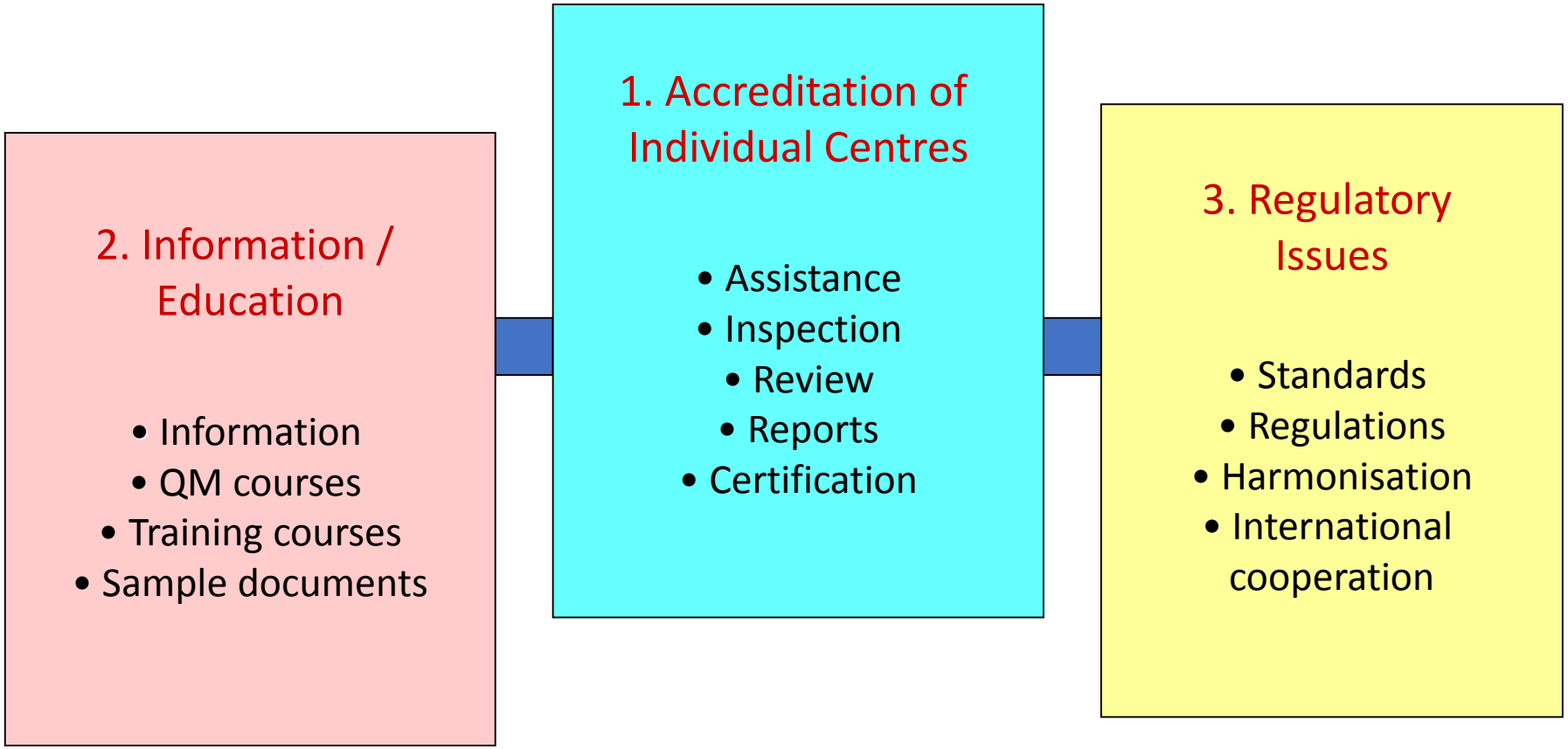
FACT/JACIE – overall umbrella

1. Clinical programme organisation
2. Ambulatory care
3. Accreditation for HLA and chimerism
4. Training, education & skills
5. Essential staffing
6. Quality, audit and benchmarking
   - Survival Outcomes Analysis
7. Recipient care
8. Donor care



B1 General	CM1 General	C1 General	D1 General
B2 Clinical Unit	CM2 Marrow Collection Facility	C2 Apheresis Facility	D2 Processing Facility
B3 Personnel	CM3 Personnel	C3 Personnel	D3 Personnel
B4 Quality Management	CM4 Quality Management	C4 Quality Management	D4 Quality Management
B5 Policies and Procedures	CM5 Policies and Procedures	C5 Policies and Procedures	D5 Policies and Procedures
B6 Allogeneic and Autologous Donor Selection, Evaluation, and Management	CM6 Allogeneic and Autologous Donor Evaluation and Management	C6 Allogeneic and Autologous Donor Evaluation and Management	D6 Process Controls
B7 Therapy Administration	CM7 Coding and Labeling of Cellular Therapy Products	C7 Coding and Labeling of Cellular Therapy Products	D7 Coding and Labeling of Cellular Therapy Products
B8 Clinical Research	CM8 Process Controls	C8 Process Controls	D8 Distribution
B9 Data Management	CM9 Cellular Therapy Product Storage	C9 Cellular Therapy Product Storage	D9 Storage
	CM10 Cellular Therapy Product Transportation and Shipping	C10 Cellular Therapy Product Transportation and Shipping	D10 Transportation, Shipping, and Receipt
			D11 Disposal
B10 Records	CM11 Records	C11 Records	D12 Records
	CM12 Direct Distribution to Clinical Program	C12 Direct Distribution to Clinical Program	

What is JACIE about?



Vital to ensure consistency of standards between centres and countries

Nurses Frontiers
www.edu-nursesnofrontiers.com
moodle

EBMT
European Society
for Blood and Marrow Transplantation


JOURNAL OF CLINICAL ONCOLOGY

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Introduction of a Quality Management System and Outcome After Hematopoietic Stem-Cell Transplantation

Alois Gratwohl, Ronald Brand, Dietger Niederwieser, Helen Baldomero, Christian Chabannon, Jan Cornelissen, Theo de Witte, Per Ljungman, Fiona McDonald, Eoin McGrath, Jakob Passweg, Christina Peters, Vanderson Rocha, Ineke Slaper-Cortenbach, Anna Sureda, Andre Tichelli and Jane Apperley

This Article

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JCO April 11, 2011 JCO.2010.30.4121

» Abstract

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Classifications

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Services


EUROPEAN HEMATOLOGY ASSOCIATION

haematologica

Journal of the European Hematology Association

Use of the quality management system "JACIE" and outcome after hematopoietic stem cell transplantation

by Alois Gratwohl, Ronald Brand, Eoin McGrath, Anja van Biezen, Anna Sureda, Per Ljungman, Helen Baldomero, Christian Chabannon, and Jane Apperley

Haematologica 2013 [Epub ahead of print]

Citation: Gratwohl A, Brand R, McGrath E, van Biezen A, Sureda A, Ljungman P, Baldomero H, Chabannon C, and Apperley J. Use of the quality management system "JACIE" and outcome after hematopoietic stem cell transplantation. Haematologica. 2014; 99:xxx doi:10.3324/haematol.2013.096461

calendar time. Overall mortality of the entire cohort of 107,904 patients with a transplant (41,623 allogeneic, 39%; 66,281 autologous, 61%) between 1999 and 2006 decreased over the 14 years observation period by a factor of 0.63 per 10 years (HR: 0.63; 0.58-0.69). This improvement was significantly faster with approx. 5.3% per year for the 49,459 patients transplanted in "JACIE" accredited centers, defined as programs having achieved accreditation the latest by November 2012, than the approx. 3.5% per year for the 58,445 patients in non accredited centers (HR: 0.83; 0.71-0.97). As a result, relapse free (HR 0.85; 0.75-0.95) and overall survival (HR 0.86; 0.76-0.98) were significantly higher at 72 months for those patients transplanted in the 162 "JACIE" accredited centers. No significant effects were observed after autologous transplants (HR 1.06; 0.99-1.13). Hence, working towards implementation of a quality management system triggers a dynamic process associated with a steeper reduction in mortality over the years and a significantly improved survival after allogeneic stem cell transplantation. Our data support the use of a quality management system for complex medical procedures.

Bone Marrow Transplantation (2015) **50,** 244–247

www.nature.com/bmt

ORIGINAL ARTICLE

The impact of improved JACIE standards on the care of related BM and PBSC donors

C Anthias[1,2], ME Ethell[3], MN Potter[3], A Madrigal[1,2] and BE Shaw[1,2,3]

Discrepancies exist between the care of unrelated donors (UDs) and related donors (RDs), particularly regarding medical suitability
ent JACIE standards have addressed these issues. We
ng 2004–2013 to determine the impact of regulatory
nation in donors not meeting UD medical suitability
res ($P=0.003$) and donor follow-up ($P=0.007$) after
rious adverse events (SAEs) in RDs not meeting UD
years ($P=0.020$). Haematopoietic progenitor cell
lity. Although changes to JACIE standards have
delines around 'grey areas' where risks to a donor are
unclear or theoretical, will be important in improving RD safety and standardising practice.

Bone Marrow Transplantation (2015) **50,** 244–247; doi:10.1038/bmt.2014.260; published online 10 November 2014

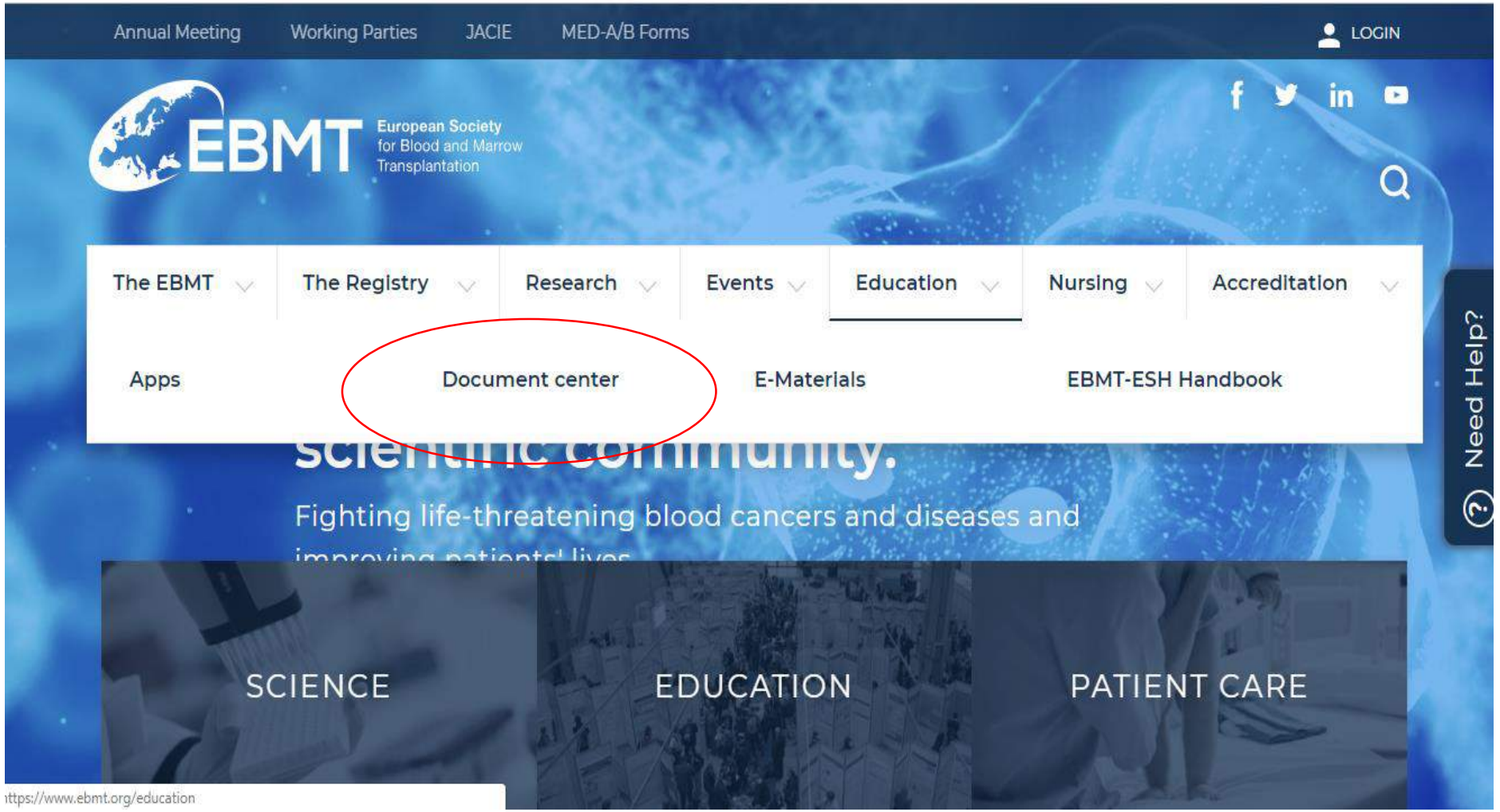
DISCUSSION

Following the introduction of JACIE standards addressing donor care, new Standard Operating Procedures were written, leading to significant improvements in donor consenting procedures and donor follow-up.

Benefits of FACT/JACIE accreditation process

- Better communication between groups of staff
- Standardisation of work practices & documentation
- Comprehensive training plan for staff implemented.
- SOPs recognised by staff as a valuable training tool.
- Sense of achievement / teamwork.
- Structured Audit Programme (previously ad hoc)
- Raised the profile of the Programme in hospital

www.jacie.org



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Differences 7th vs 6.1th

Negligible: 58

Minor: 32

Moderate: 16

Significant: 6

New: 25

Reorder: 7

Bone Marrow Transplantation (2003) 31, 417–421

www.nature.com/bmt

Review

Transplant center characteristics and clinical outcomes after hematopoietic stem cell transplantation: what do we know

FR Loberiza Jr[1], DS Serna[1], MM Horowitz[1,2] and JD Rizzo[1,2]

[1]*International Bone Marrow Transplant Registry, Health Policy Institute, Medical College of Wisconsin, Milwaukee, WI, USA; and* [2]*Division of Neoplastic Diseases and Related Disorders, Department of Internal Medicine, Medical College of Wisconsin, Milwaukee, WI, USA*

Center effects are differences in outcome among treatment centers that cannot be explained by identifiable differences in patients treated or specific treatments applied and are presumed to result from differences in the ways health care is delivered.

Training and experience of personnel, availability of resources and characteristics of center organization.

Individual center characteristics may not be equally important (or important at all) for optimal patient outcomes.

Professional Competencies

STANDARD:

C4.3 The Quality Management Plan shall include, or summarize and reference, personnel education, experience, and training requirements for each key position in the Apheresis Collection Facility. Personnel requirements shall include at a minimum:

C4.3.1 Current job description for all staff.

C4.3.2 A system to document the following for each staff member:

C4.3.2.1 Initial qualifications.

C4.3.2.2 Orientation.

C4.3.2.3 Initial training.

C4.3.2.4 Competency for each critical function performed.

C4.3.2.5 Continued competency at least annually.

C4.3.2.6 Training and retraining.

C4.3.2.7 Provisions for continuing education.

C4.3.3 A description of minimal trainer qualifications and a uniform plan for staff training.

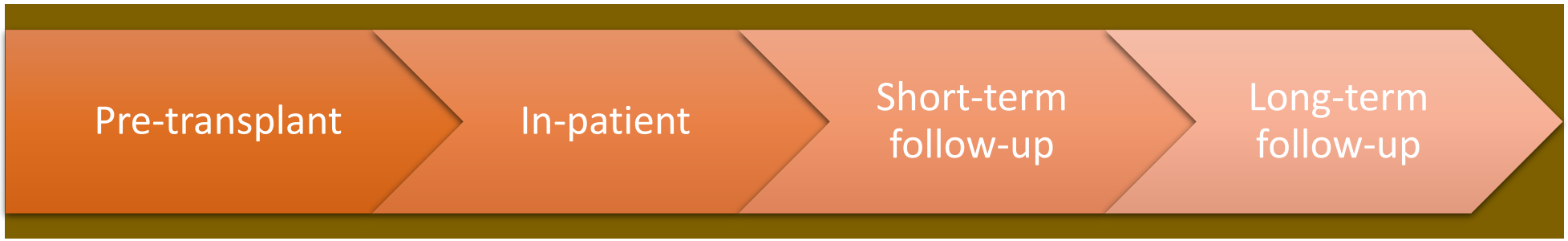
Where nurses competencies are needed?

General roles

- Nurse as patient advocate….
- Commitment to providing high quality care
- Experience and knowledge
- Critical-analytical thinking & problem solving

SCT specific roles

- Present at different time points
- Different nursing roles
- Promoting evidence based practice in SCT care
- SCT Quality management processes



Nurses Frontiers
www.edu-nursesnofrontiers.com
moodle

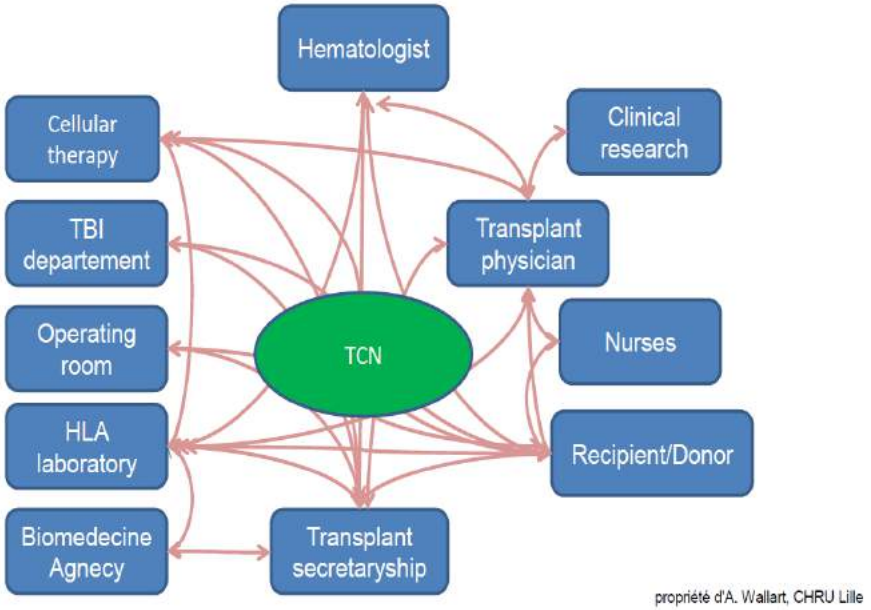
EBMT
European Society
for Blood and Marrow Transplantation

Table 2 Nurses' requirements in 7th edition

B3.7	NURSES	No change
B3.7.1	The Clinical Program shall have nurses formally trained and experienced in the management of patients receiving cellular therapy.	No change
B3.7.2	Clinical Programs treating pediatric recipients shall have nurses formally trained and experienced in the management of pediatric patients receiving cellular therapy.	Negligible
B3.7.3	Nurses shall have received specific training and maintain competence in the transplant-related skills that they routinely practice including:	Minor
B3.7.3.1	Hematology/oncology patient care, including an overview of the cellular therapy process.	No change
B3.7.3.2	Administration of preparative regimens.	No change
B3.7.3.3	Administration of blood products, growth factors, cellular therapy products, and other supportive therapies.	No change
B3.7.3.4	Care interventions to manage cellular therapy complications, including, but not limited to, cytokine release syndrome, tumor lysis syndrome, cardiac dysfunction, respiratory distress, neurologic toxicity, macrophage activation syndrome, renal and hepatic failure, disseminated intravascular coagulation, anaphylaxis, neutropenic fever, infectious and noninfectious processes, mucositis, nausea and vomiting, and pain management.	Moderate (mostly related to immuno-effector cells)
B3.7.3.5	Recognition of cellular therapy complications and emergencies requiring rapid notification of the transplant team.	No change
B3.7.3.6	Palliative and end of life care.	No change
B3.7.4	There shall be written Standard Operating Procedures or guidelines for nursing procedures, including, but not limited to:	Negligible
B3.7.4.1	Care of immunocompromised recipients.	Negligible
B3.7.4.2	Age-specific considerations.	new

B3.7.4.3	Administration of preparative regimens.	No change
B3.7.4.4	Administration of cellular therapy products.	No change
B3.7.4.5	Administration of blood products.	No change
B3.7.4.6	Central venous access device care.	No change
B3.7.4.7	Detection and management of immune effector cellular therapy complications including, but not limited to, those listed in B3.7.3.4.	No change
B3.7.5	There shall be an adequate number of nurses experienced in the care of transplant recipients.	Negligible
B3.7.6	There shall be a nurse/recipient ratio satisfactory to manage the severity of the recipients' clinical status.	Negligible

Complex network - nurses management
Nurses competencies are mandatory



Transplant Coordinator Nurse evolution

- HSCT process is complex
- Patient management strategies can:
  - **Promote patient focused care**
  - **Assist in planning and organisation of care**
  - **Facilitate high quality care delivery**
  - **Aid in developing research / evidence based care**
- Nurses have a key role in all aspects of patient management!

First-step certification

- Based on FACT-JACIE Standards
- Aimed at LMICs
- Goal is to build capacity in BMT centres
  - To work with quality/safety
  - To seek full accreditation

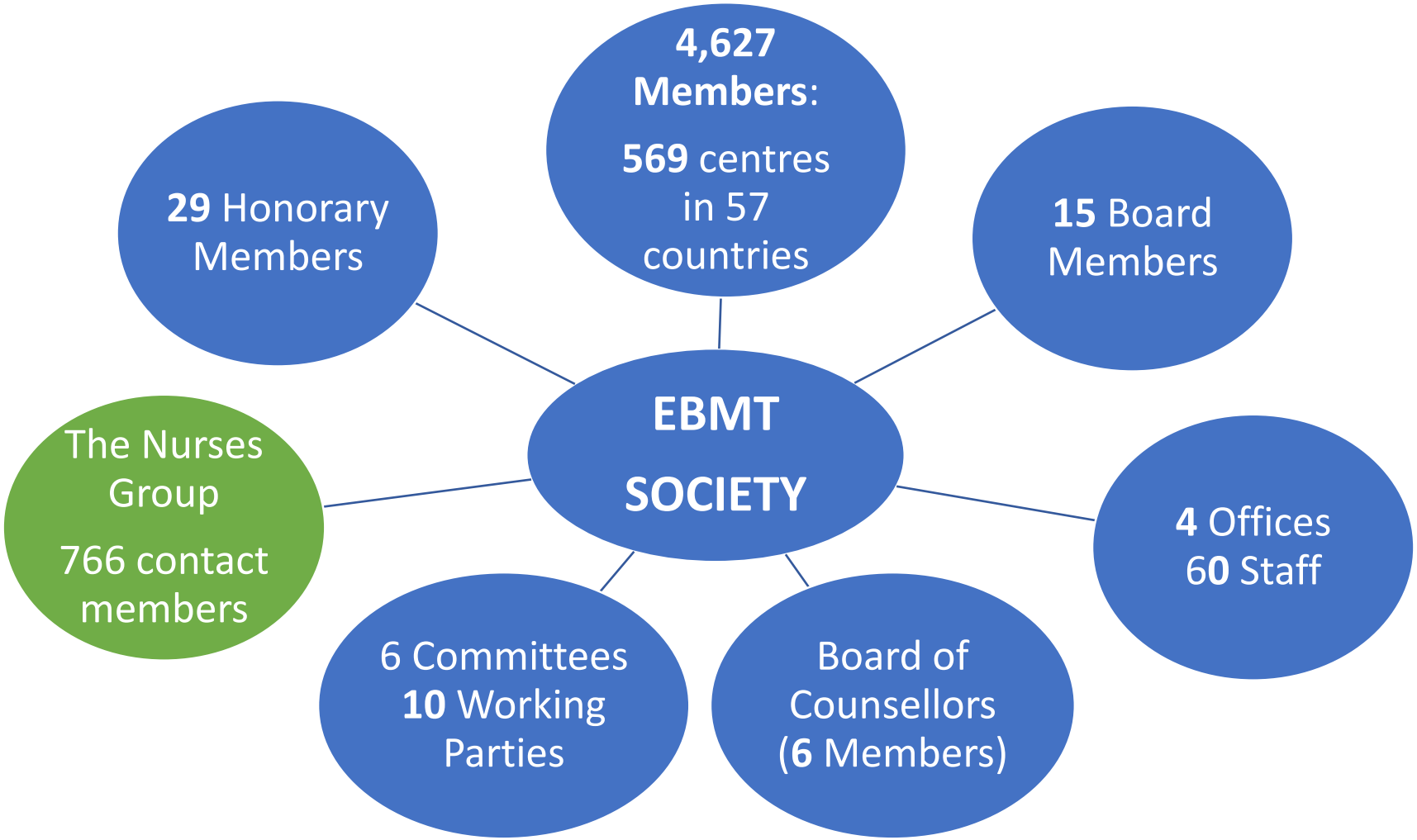
EBMT Nurses Group Overview

Aleksandra Babic, EBMT Nurses Group Global Educational Committee Chair

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

Background & Introduction



Background & Introduction

- EBMT Nurses Group is the leading group in the field of Haematology and Haematological Stem Cell Transplantation nursing.

- Dedicated to improving the care of patients receiving HSCT and work towards promoting excellence in care by supporting nurses and health care professionals in recognizing, building upon and providing evidence based practice.

- EBMT NG Mission is to enhance and value the nurses role all over the world, supporting and sharing knowledge through;
  - communication,
  - advocacy,
  - research,
  - training,
  - education

The EBMT Nurses Group organisation

- The NG have **766** contact members in **57** countries
- Collaborations between Canada and USA are being pursued

- The EBMT NG is settled with many National Groups:
  - **Austria**
  - **Belgium**
  - **EMBMT forum(Algeria, Egypt, Iran, Jordan, Lebanon, Morocco, Oman, Pakistan, Saudi Arabia, Syria, Tunisia)**
  - **France**
  - **Germany**
  - **Switzerland**
  - **Italy**
  - **Nordic Forum (Denmark, Finland, Iceland, Norway, Sweden)**
  - **Spain**
  - **The Netherlands**
  - **United Kingdom**
  - **Turkey**
  - **Czech Republic**
  - **EAST forum (in reconstruction)**
  - **Greece – work in progress 2016**
  - **India?**

Board members:

President – John Murray (UK); Secretary – Michelle KENYON (UK) ; Account Officer – Aleksandra Babic (CH)

1. **Research Committee – Chair Sarah Liptrott (IT)**

   Aims to coordinate and lead the development of research programs in BMT/SCT.

2. **Communication & Networking Committee – Chair Alberto CASTAGNA (IT)**

   Works with the EBMT Communication Coordinator on the development and production of the Newsletter.

3. **Scientific Committee – Chair Simone VAN DER LINDEN (NL)**

   Coordinates and organizes the annual conference, including satellite symposia and the pre meeting education day.

4. **Pediatric Committee – Chair Daphna Hutt (IS)**

   Aims to improve the care of pediatric and adolescent SCT patients and to promote, develop and share knowledge between pediatric nurses.

5. **Global Education Committee - Chair Aleksandra Babic (CH)**

   Aims to contribute to the fostering of excellence and inform on developments within BMT in LMIC.

Achievements GEC 2017-2018

Program
Training course for HSCT nurses -draft
December, 8th -9th 2017
Location: Myanmar, Yangon

8th December 2017 • Theoretical presentation	
08:00 – 08:20 (20m)	Welcome and introduction Local authorities
08:20 – 09:00 (40m)	Michelle Kenyon (UK) Transplants, Principles of Conditioning & Cell infusion
09:00 – 09.30	Aleksandra Babic (Switzerland) PSC Mobilization and Apheresis
09.30 – 10.10 (40m)	Julia Ruiz (ESP) Nurses care of immunosuppressed BMT patients (adult and children) Infection risks: Hygiene, isolation & hand washing Infections and infection control
10:10 – 10.40	Break
10.40-11.10	Eugenia Trigoso (ESP) Nutrition control in children & Low bacterial diet
11.10 – 11.50 (40m)	Alberto Castagna (IT) Early and acute HSCT complication and nurses care in children and adult Mucositis & Oral Care
11:50 – 12:30 (40m)	Julia Ruiz (ESP) Nursing management of Graft Versus Host Disesas (GVHD)
12:30 – 14:00	Lunch
14.00 – 14:40 (40m)	Eugenia Trigoso (ESP) Nursing Management of Haemorrhagic Cystitis Michelle Kenyon (UK) Nursing Management of Hepatic Veno-occlusive disease (VOD)
14:40 – 15:30 (50m)	Case based panel discussion
15:30 – 16.00	Break
16.00 – 16.40 (40m)	Michelle Kenyon (UK) Quality of Life post BMT Eugenia Trigoso (ESP) Palliative care
16.40	End of day 1
	9th December 2017 • Practical course in hospital or auditorium
09:00 – 11:00 (120m)	MAURO Pittiruti (IT) PICC – Peripherally inserted central line- practical course and CVC management Demonstration –PICC positioning/flushing, dressing – (physicians are welcome too) -
11:00 – 12.30	Case based panel discussion
12.30 – 14.00	Lunch
14.00 – 14.40 (40m)	Hospital visit

THE REPBULIC OF THE UNION OF MYANMAR
MINISTRY OF HEALTH AND SPORTS
DEPARTMENT OF MEDICAL SERVICE
YANGON CHILDREN HOSPITAL

Letter No. ২৩ / KALASAYA(1130) 2017
Date of Issue: July 12, 2017

- Invitation from Prof Aye Aye Khaing
- Paed program: Contacts with nurse from Boston who volontiered in Yangon children hospital
- Autologous transplant ongoing in Yangon and Mandalay
- Interest from national network, but financial difficulties
- One nurse represent has been invited to attend the next annual EBMT conf. 2019

Global Educational Committee

First Training Course for HSCT Nurses

Aleksandra Babic[1], Alberto Castagna[2], Michelle Kenyon[3], Mauro Pittiruti[4], Julia Ruiz[5] & Eugenia Trigoso[6]

[1]Oncology Institute of Southern Switzerland-IOSI. Bellinzona, Switzerland. [2]Hospital Policlinico-AOUI. Verona Italy. [3]King's College Hospital. London, UK. [4]Università Cattolica del Sacro Cuore. Roma, Italy. [5]Hospital Infanti Universitario Niño Jesus. Madrid, Spain. [6]Hospital Universitario y Politécnico LA FE. Valencia, Spain.

INTRODUCTION & BACKGROUND

Nurses Non Frontiers and EBMT NG Global Committee in collaboration with Childhood Cancer International and Yangon Children's Hospital organised the first training course for HSCT nurses in Yangon, Myanmar in December 2017.

Myanmar is a lower-middle-income country in Southeast Asia, with a diverse cultural and socioeconomic background and variable communication and transport obstacles. Up until 2012, childhood cancer management was particularly challenging, with a scarcity of human resources, quality improvement initiatives, and limited treatment outcomes. There have been only 2 centers for childhood cancer treatment in Myanmar: Yangon Children's Hospital and Mandalay Children's Hospital (Hnin, T.M., *et al.* 2017).

OBJECTIVES

The National Cancer Control Plan launched The National Childhood Cancer Action Plan for 2017-2021 that includes the increase of committed and trained health care providers. Several workforce training has been ongoing with international conferences, and on-site continuing education lectures from international visitors.

The EBMT NG Global Committee contributed with this training in the field of of Haematology and Haematopoietic Stem Cell Transplantation, to improve knowledge and skills for adult HSCT, and settle first learnings for paediatric HSCT as at the moment this programme has not been established.

METHODS

A questionnaire in order to assess nurses education, patient assessment knowledge and learning preference, was distributed months before the meeting.

Training course was held in two days:

- First day, December 8th, with front lesson presentations - focused on evidence based quality of care in BM transplant, on principles of conditioning, nutrition control, BMT complications management such as, Mucositis, GvHD, Haemorrhagic Cystitis and infection control and risk.
- The second day, December 9th, a practical course on central venous devices management was held by Mauro Pittiruti, particularly focused on peripherally inserted central lines (PICCs), with large participation of doctors from different hospitals across the country.

We also visited Yangon Children's Hospital, paediatric ward, laboratory and blood bank.

RESULTS

Over a hundred nurses together with some physicians, attended from Yangon Children's Hospital, Mandalay Children's Hospital, and satellites centers, and they were extremely interested, especially on BMT complications.

Most nurses are Diploma and Bachelor's degree, Master's degree course is available, but nurses don't have the opportunity to attend it currently.

Our educational course was a stepping stone, indicating to local nurses JACIE oriented direction on how to implement their learning priorities in the future.

CONCLUSION

The future plans within the National Childhood Cancer Action Plan, are to continue and strengthen the workforce and promote effective definitive treatment and supportive care.

Workforce continuing education has been established based on online continuing education with international hospital partners. EBMT NG Global Committee is looking forward to collaborate and establish an online continuing education focused on HSCT issues. For that reason we look forward to continue our collaboration with a second step, an advanced training course focused on management of adult and paediatric patients undergoing BMT, using the new technologies possibilities such as on-line follow up, courses.

India – structured project 2018-2021

REPORT ON NATIONAL TRAINING PROGRAMME FOR BMT NURSES

With a objective to promote an overview of BMT and discuss various trends in BMT Nursing, we the Nursing Department at Advanced Centre for Treatment, Research and Education in Cancer (ACTREC) along with European Bone Marrow Transplant Nursing team (EBMT) & Nurses No Frontiers organized a 2 days National Training Programme for BMT Nurses on 9th & 10th of December 2016 at ACTREC, Kharghar, Navi Mumbai, India.

- Collaboration started in 2016
- Over 200 nurses participants
- Strong local partner - University Gov. Hospital – biggest in Asia
- Meera Achrekar- EBMT NG contact
- Intent to built the Nurses National Group linked with the EBMT – membership fee reduced

→ Stepstone for ongoing education project: first level JACIE educational courses

Ongoing projects update

Indian Study Objective: to understand if EBMT NG educational courses increase nurses competencies in BMT setting in India?

- India is one of the LMICs in rapid evolvement with 75 transplant centers officially reporting their activities to national registry.
- EBMT NG Board and GEC is in contact with local authorities in order to support the formation of the Indian BMT Nurses Group Network and to establish the educational program for nurses in line with JACIE standards -> supported by JACIE office.
- In collaboration with NG RC
- Proposal -3 phases:
  - Phase 1 Survey (S1) : Identify current clinical practice, educational gaps linked to JACIE standards:

    Group A (all Indian BMT centers) vs Group B (educational course participants (S1+S2))
  - Phase 2: deliver the EBMT NG educational course that meets JACIE standards. (December 14th and 15th)
  - Phase 3 Compare results of the participants group (GROUP B-(S2)) with the results of the Survey sent to all Indian centers (GROUP A (S1))

EBMT European Society for Blood and Marrow Transplantation

Indications for HPC Transplantation - autologous and allogeneic

Michelle Kenyon
Consultant Nurse (BMT)

EBMT Training course
Mumbai, India
14th and 15th December 2018

Learning outcomes

Standard indications

Experimental indications

Understand pre-transplant considerations

- Transplant types
- Donor selection

Understand principles of conditioning therapy

- Purpose
- Rationale for therapy selection (myeloablative, RIC, haplo)

Understand principles of cell infusion

- Procedural considerations
- Process review/ audit

“ ***STANDARD:*** *Indications for allogeneic and autologous HPC transplantation.*

Explanation:

Clinical Program Directors and attending physicians who perform only autologous transplants must be competent to recognize when an allogeneic transplant is indicated. ”

Transplant process – sequence of events

Gain informed consent from recipient (& donor)
Verify ***availability and suitability*** of donor or cellular product ***before*** initiating recipient preparative regimen
Administer preparative regimen (conditioning)
Administer cellular therapy product (transplant)
Monitor for early effects & provide supportive care
Plan safe discharge
Assess for aGvHD and cGvHD (in allogeneic setting)
Monitor for post-transplant late effects

Transplant indications

current indications

- Regularly updated
- Cover haematopoietic SCT for haematological diseases, solid tumours and immune disorders
- Reflect major changes in the field of haematopoietic SCT
- Include indications for cord blood units as well as haploidentical donors continuous refinement of conditioning strategies has expanded the number of potential indications as well as consideration of older patients or those with co-morbidity for transplant
- https://www.nature.com/articles/bmt20156#t1

experimental indications

- accumulating evidence of the role of haematopoietic SCT in non-haematological disorders such as autoimmune diseases
- the advent of new drugs and effective targeted therapy has challenged the role of SCT in some instances

https://www.nature.com/articles/bmt20156#t1

Indications example AML

Disease	*Disease status*	*Sibling donor allo-HSCT*	*Well-matched URD allo-HSCT*	*Alternative donor allo-HSCT*	*ASCT*
AML	CR1 (low risk)[a]	CO/II	D/II	GNR/II	CO/I
	CR1 (intermediate)[a]	S/II	CO/II	D/II	S/I
	CR1 (high risk)[a]	S/II	S/II	CO/II	CO/I
	CR2	S/II	S/II	CO/II	CO/II
	CR3, incipient relapse	S/III	CO/III	D/III	GNR/III
	M3 Molecular persistence	S/II	CO/II	GNR/III	GNR/III
	M3 Molecular CR2	S/II	CO/II	GNR/III	S/II
	Relapse or refractory	CO/II	CO/II	D/II	GNR/III

CO = clinical option, can be carried after careful assessment of risks and benefits
D = developmental, further trials are needed
GNR = generally not recommended;
S = standard of care generally indicated in suitable patients

Standard of care (S)

- indications categorised as ‘standard of care’ are reasonably well defined and results compare favourably (or are superior) to those of non-transplant treatment approaches
- does not mean an HSCT is necessarily the optimal therapy for every patient in all clinical circumstances

Clinical option (CO)

- for many indications, number of patients will be low and randomized studies comparing conventional treatment and HSCT difficult to perform
- results of small patient cohorts treated by HSCT show efficacy and acceptable procedure related toxicities
- current interpretation of existing data for indications placed in CO supports HSCT as valuable option for individual patients after careful discussion of risks and benefits
- needs further evaluation for groups of patients

Developmental (D)

- limited experience in combination with the type of transplant and additional research is needed to define the role of HSCT
- transplants should be done within the framework of a clinical protocol
  - Eg randomized comparison of two or more approaches to treatment or a small pilot series
- category covers new approaches to management of a disease that, in a different stage, may already be classified under the standard of care or clinical option
- protocols for ‘developmental’ transplants will have been approved by local research ethics committees and must comply with current international standards

Generally not recommended (GNR)

- can include early disease stages when results of conventional treatment do not normally justify additional risk of NRM, or when the disease is so advanced that the chance of success is so small that the risk of the harvest procedure for the normal donor is difficult to justify
- also includes HSCT for a disease in a phase or status in which patients are conventionally not treated by HSCT
- there will be some overlap between GNR and D, and further research might be warranted within prospective clinical studies for some of these indications

Pre-transplant considerations

STANDARD:

B3.3.4.2 Selection of suitable recipients and appropriate preparative regimens.

B3.3.4.3 Donor selection, evaluation, and management.

Explanation:

Donor selection, evaluation, and management may be the responsibility of one or more than one clinical team. If responsibilities are divided, documented communication between teams is required.

Which type of transplant?

Depends on recipient

- Age
- Disease
- Co-morbidities
- (ability to harvest stem cells)

Depends on donor

- Availability
- Fitness to donate
- Cell source

Stem cell sources

Autologous

- Cells are harvested **from the patient** and re-infused after conditioning
- Cells are usually harvested from the blood

Allogeneic

- Cells are harvested **from a donor** and re-infused to the patient after conditioning
- Cells are usually harvested from the blood but bone marrow is sometimes used

related donor

- Matched sibling
- Haplo-identical (parent, child, 'half-matched' sibling)

unrelated donor

- Matched unrelated
- Mismatched unrelated
- Umbilical cord

Donor searching

HLA typing patient and siblings

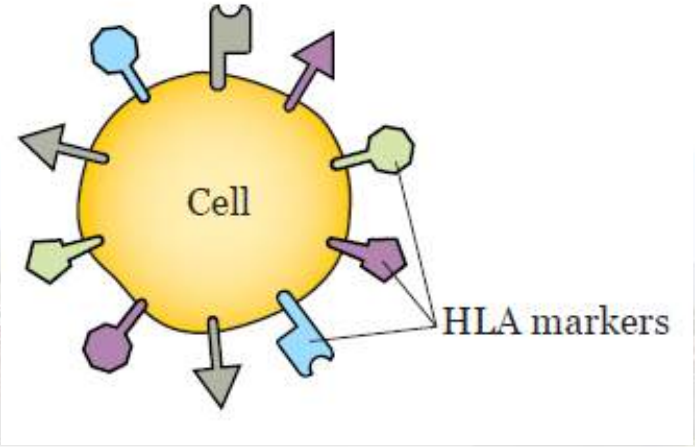
- HLA are proteins (or markers) found on most cells in the body
- immune system uses the markers to recognise which cells belong in your body and which do not

Initiate search for unrelated donor

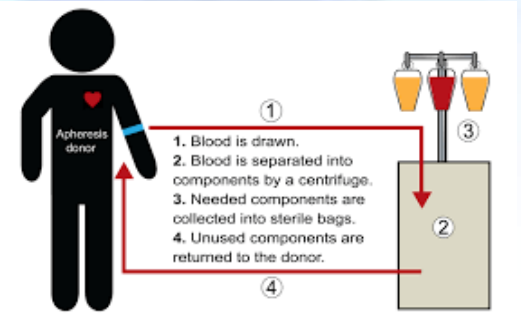
Consider cord or haplo

National registry often quicker than overseas

- For medical assessment
- Cell procurement/ cost



Donor evaluation



- independent assessment – related donor
- medical and clinical evaluation
- informed consent
- blood profile to be completed within 28 days of planned collection
- cell collection timed for day 0
- if transplant delayed, for unrelated donors need to seek ‘medical exception’ from registry director to store cells
- subsequent collection such as DLC will necessitate repeat blood work-up and consent

STANDARD:

B3.3.4.4 Donor and recipient informed consent.

B3.3.4.5 Administration of preparative regimens

B3.3.4.6 Administration of growth factors for HPC mobilization and for post-transplant hematopoietic cell reconstitution.

B3.3.4.7 Cellular therapy product administration and patient management.

Example(s):

The requirement for training and competency in HPC product administration and patient management may be documented with copies of administration reports for each physician or by competency evaluations developed by the Clinical Program

Considerations prior to transplantation

Recipient

- remission status
- co-morbidities
- psychological well-being

Donor

- availability
- suitability
- care provided by different clinical team
- clearance – medical fitness
- informed consent

Recipient preparation

- fertility preservation
- physical/ medical assessment
  - Organ assessment
  - Disease assessment
- CVC insertion
  - Hickman
  - PICC
- psychosocial assessment (HNA)
  - financial support
  - carer support
- informed consent

Pre-transplant - nursing considerations

Supporting informed consent

- information provision
  - verbal, written, multi-media
- answer questions (patient and carers)
- check understanding
- arrange further consultations if needed
- manage expectation

Maintaining care

- CVC care
- supportive care
  - transfusions
  - antibiotics
  - symptom management

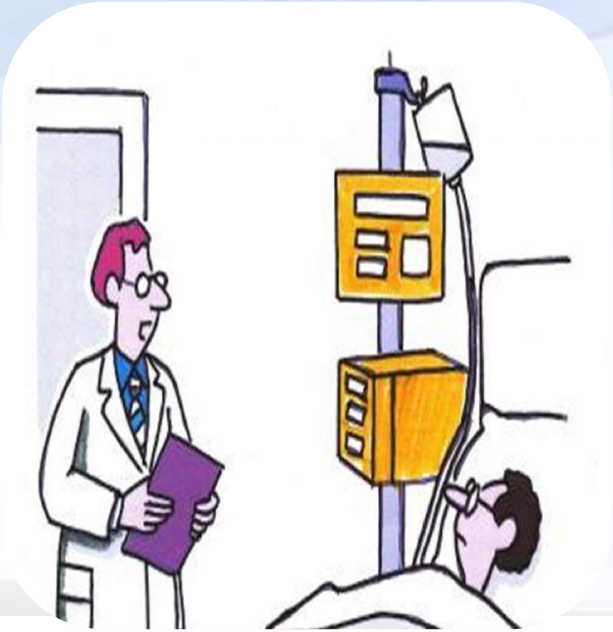
BMT Co-ordinator CNS

Identify and address unmet needs

which conditioning for which transplant

Conditioning therapy

- combination of agents or approaches
  - biologic
  - radiologic (TBI)
  - chemotherapy
- agents, dosing and intensity depend on
  - disease
  - patient comorbidities
  - type of transplant
- duration of conditioning between 1-10 days
- patients hospitalised or ambulatory
- side effects often last several weeks



Aims of conditioning

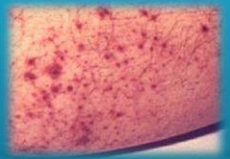
One or more of the following

- destroy any existing cancer cells or abnormal cells
- stop the recipient immune system working to reduce risk of the transplant being rejected
- destroy existing bone marrow cells to make room for the transplanted tissue

Common immediate effects of conditioning

tiredness

skin rashes



hair loss (alopecia)

infections/protective isolation

GI issues

- nausea & vomiting
- loss of appetite
- mouth ulcers/ **mucositis**
- diarrhoea

Mouth ulcers and skin rashes usually improve on engraftment
Hair usually starts to grow back around three months

Cell infusion

Product characteristics

Cell source (BM, PB, CB)
- Cell counts
- Volume

Number of bags (DMSO toxicity) >1 cell infusion day

ABO compatibility (Allogeneic cell)

Fresh vs thawed infusion
- Crypotectant DiMethylSulphOxide (DMSO) enables cell freeze and thaw without membrane damage

Where cellular products > one donor, infuse first product safely before administering second

Cell administration

infuse each bag quickly – 10-15 mins
do not add or infuse any solutions through the same tubing with the product
DO NOT irradiate

1

Timing

identify appropriate time between last day of preparatory regime and cellular product infusion

2

Patient preparation

pre-med hydrocortisone, chlorpheniramine, paracetamol, fresh wide bore giving set primed with saline

observe for adverse reactions (hypoxia, bradycardia, hypertension)

record vital signs

information, reassurance and comfort

3

Verification process

confirm identity of intended recipient and product container

inspect product integrity and appearance of contents

agitate product container to mix contents

Patient care during administration

- often feeling unwell due to conditioning
- cell infusion marks an important milestone for every patient – remember to make them feel comfortable ….and special
- advise what to expect
- give clear explanations
- reassure

Every year I celebrate my transplant birthday and feel amazed that someone generously gave me such a valuable gift of life

EBMT European Society for Blood and Marrow Transplantation

Thanks!

Any questions?

@michellekenyon5

michelle.kenyon@nhs.net

ebmt.org

Patient care: Isolation- DPI

Julia Ruiz, Spain

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

INTRODUCTION. ISOLATION

GUIDES FOR PATIENTS: INFORMATION ABOUT TRANSPLANT PROCESS

Psychooncology. 2013 Aug;22(8):1790-7. doi: 10.1002/pon.3215. Epub 2012 Nov 7.

Predictors of anxiety and depression in hematopoietic stem cell transplant patients during protective isolation.

Tecchio C[1], Bonetto C, Bertani M, Cristofalo D, Lasalvia A, Nichele I, Bonani A, Andreini A, Benedetti F, Ruggeri M, Pizzolo G.

Author information

Abstract

OBJECTIVE: To examine in a sample of hematopoietic stem cell transplant patients assessed throughout protective isolation (i) levels of anxiety and depression and (ii) pre-isolation factors (socio-demographics, biomedical variables and personality traits), which might predict higher levels of anxiety and depression during isolation.

METHODS: The study used a longitudinal prospective design. Anxiety and depression were assessed in 107 participants by the State-Trait Anxiety Inventory and Self-rating Depression Scale at admission and weekly at fixed time points throughout isolation. Among pre-isolation factors, patients' psychological status was evaluated by the Cognitive Behavioral Assessment (2.0). Predictors were explored by random-effects models.

RESULTS: One-tenth of the patients suffered from clinically significant anxiety and depressive symptoms at admission. Although the percentage of depressed patients increased more than twofold after 2 weeks of isolation, that of anxious patients did not significantly change over time. Female gender, higher anxiety and obsessive-compulsive symptoms, intratensive personality traits and lower performance status predicted higher depression during isolation.

CONCLUSIONS: Anxiety and depression represent a relevant problem for hematopoietic stem cell transplant patients during isolation. Early detection of predictors, such as anxiety levels, obsessive-compulsive symptoms and performance status, could help prevent depression via targeted psychological intervention.

J Clin Nurs. 2017 Dec;26(23-24):4467-4478. doi: 10.1111/jocn.13777. Epub 2017 Apr 7.

Being in protective isolation following autologous haematopoietic stem cell transplantation: A phenomenological study.

Biagioli V[1], Piredda M[2], Annibali O[3], Iacorossi L[4], D'Angelo D[2], Matarese M[2], Alvaro R[1], De Marinis MG[2].

Author information

Abstract

AIMS AND OBJECTIVES: To explore the lived experiences of patients with haematological malignancies who had been in protective isolation during their hospital stay for autologous haematopoietic stem cell transplantation.

BACKGROUND: Although protective isolation aims to benefit patients' health by preventing infection, it could also imply harmful psycho-social implications for patients, such as loneliness.

DESIGN: A descriptive phenomenological study was conducted in an Italian university hospital.

METHODS: Nine patients with haematological malignancies who had been in protective isolation for autologous haematopoietic stem cell transplantation were enrolled. They were interviewed during their weekly ambulatory visits, which are usually carried out up to 100 days post-transplant, and asked about their stay in isolation. Giorgi's method of analysis was used to describe the experience of protective isolation from the patient' perspective.

RESULTS: Eight themes emerged: isolation is a defence, threats from which patients have to defend themselves, rules for defence, the burden of the defence, external strategies for defence, inner strengths for defence, defending loved ones and outcomes of the defence. The general structure was expressed as a defence from suffering.

CONCLUSIONS: While fighting a hard battle against cancer, informants largely accepted the strict isolation measure and represented it as a shield for an effective defence.

RELEVANCE TO CLINICAL PRACTICE: Nurses should provide emotional and social support to help patients feel like active fighters and strengthen their strategies for an effective defence from suffering.

Nurse support
Psychological support
Family support

ESSENTIAL FACTS FOR TRANSPLANT PATIENTS

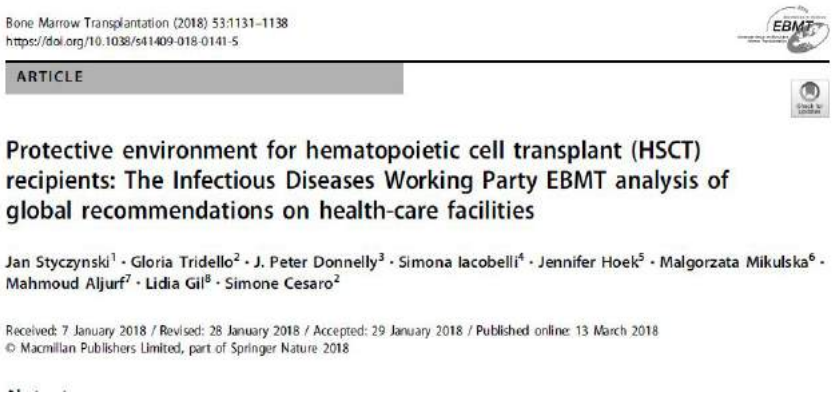
EVIDENCE BASED PRACTICE. ISOLATION JACIE

B2.1 There shall be a designated inpatient unit of appropriate location and adequate space and design that minimizes airborne microbial contamination.

This standard does not require that every clinical unit have laminar airflow availability, but HEPA filtration with positive pressure is recommended for high-risk patients

Further, auditing of airborne microbial infections in non-HEPA rooms should be performed as part of the QM Program.

Clinical Program must have policies and SOPs that define infection control requirements based upon differing patient conditions and room configurations



Bone Marrow Transplantation (2018) 53:1131–1138
https://doi.org/10.1038/s41409-018-0141-5

ARTICLE

Protective environment for hematopoietic cell transplant (HSCT) recipients: The Infectious Diseases Working Party EBMT analysis of global recommendations on health-care facilities

Jan Styczynski[1] · Gloria Tridello[2] · J. Peter Donnelly[3] · Simona Iacobelli[4] · Jennifer Hoek[5] · Malgorzata Mikulska[6] · Mahmoud Aljurf[7] · Lidia Gil[8] · Simone Cesaro[2]

Received: 7 January 2018 / Revised: 28 January 2018 / Accepted: 29 January 2018 / Published online: 13 March 2018

Knowledge on the details and maintenance of protective environments in the HSCT setting was inadequate reflecting a lack of communication between the health personnel involved, hospital infection control and the hospital maintenance services

EVIDENCE BASED PRACTICE. ISOLATION

Table 1 Overall positive results of the survey with respect to Global Recommendations GRPE

Protective environment recommendation	Grading[a]	Survey question (Q)	Positive response	Total (%)
1. Ventilation: ≥12 air changes per hour.	AIII	Does the room have at least 12 air changes per hour? (Q9)	Yes	126 (71.2%)
2. Central or point-of-use HEPA filters with 99.97%efficiency for removing particles ≤0.3 μm in diameter.	AIII	Are your patient rooms equipped with HEPA filters? (Q6)	Yes	176 (99.4%)
		If yes, please specify (Q7)	Central	81 (45.8%)
			Local	85 (48.0%)
		Do you have HEPA filters with 99.97% efficiency for removing particles ≤0.3 μm in diameter? (Q12)	Yes	124 (70.1%)
3. Filters should be replaced regularly based on manufacturers' recommendations, and, when there is ongoing construction, filtration efficiency should be monitored frequently to best determine appropriate time for replacement.	AIII	How often are the filters changed? (Q14)	Regularly	52 (48.6%)[b]
		Do you have a written procedure for filter maintenance and removal? (Q15)	Yes	95 (53.7%)
4. Directed airflow so that air intake occurs at one side of the room and air exhaust occurs at the opposite side.	BIII	Is the airflow directed so that air intake occurs at one side of the room while the air exhaust occurs at the opposite side? (Q18)	Yes	105 (59.3%)
5. Consistent positive air pressure differential between the patient's room and the hallway ≥2.5 Pa (i.e., 0.01 inches by water gauge).	BIII	Is there a permanently installed device / mechanism to constantly monitor the differential air pressure between the room and the corridor? (Q20)	Yes	68 (38.4%)
		What is the pressure in the anteroom? (Q23)	Positive	34 (19.2%)
		Is there an air pressure monitoring device / mechanism in the anteroom in addition to the patient's room? (Q24)	Yes	31 (17.5%)
6. Well-sealed rooms (e.g., filling the gaps between walls and windows, outlets, floor, and ceiling) should always be used for HCT patients to prevent infiltration of air from outside the room that could allow entry of spores and hinder maintenance of proper pressure differential.	BIII	Are the room windows sealed to eliminate infiltration from outside? (Q27)	Yes	125 (70.6%)
		Do the protective environment rooms have monolithic ceilings? (Q28)	Yes	62 (35.0%)
		Are all plumbing pipes in the room sealed around wall penetrations? (Q29)	Yes	91 (51.4%)
7. Continuous pressure monitoring, especially while rooms are occupied.	BIII	Is there a monitoring system that will set off an alarm when the pressure differential between any protective environment room and adjacent hallway or anteroom falls to less than 2.5 Pa to alert staff to possible engineering failures? (Q34)	Yes	60 (33.9%)
8. Self-closing doors to maintain constant pressure differentials.	BIII	Are there self-closing doors to maintain constant pressure differentials? (Q33)	Yes	66 (37.3%)
9. Consideration should be given to using monitoring systems that will set off an alarm when the pressure differential between any protective environment room and adjacent hallway or anteroom falls to less than 2.5 Pa, to alert staff to possible engineering failures.	CIII	Is a sensor monitor installed in the patient room used to determine when the HEPA filters require changing? (Q13)	Yes	32 (18.1%)
10. To enable the nursing staff to observe the HCT recipient even when the doors are closed, windows can be installed in either the door or the wall of the HCT recipient's room.	CIII	Are the nursing staff able to observe the patient even when the doors are closed? (Q35)	Yes	109 (61.6%)

[a]Grading according to [1, 3]

[b]Answers to Q14 were provided only when answer to Q13 was "no" ($n = 107$)

Protective environment for haematopoietic cell transplant recipients

EVIDENCE BASED PRACTICE. ISOLATION

ISOLATION

PROTECTIVE ENVIRONMENT

Patients: allogeneic hematopoeitic stem cell transplant (HSCT)

- Maintain in PE room except for required diagnostic or therapeutic procedures that cannot be performed in the room, e.g., radiology, operating room
- Respiratory protection e.g., N95 respirator, for the patient when leaving PE during periods of construction

Standard and Expanded Precautions

- Hand hygiene observed before and after patient contact
- Gown, gloves, mask NOT required for HCWs or visitors for routine entry into the room
- Use of gown, gloves, mask by HCWs and visitors according to Standard Precautions and as indicated for suspected or proven infections for which Transmission-Based Precautions are recommended

Engineering

- Central or point-of-use HEPA (99.97% efficiency) filters capable of removing particles 0.3 µm in diameter for supply (incoming) air
- Well-sealed rooms: windows, doors, ceilings, no leakages.

EVIDENCE BASED PRACTICE. ISOLATION

ISOLATION

PROTECTIVE ENVIRONMENT

Engineering

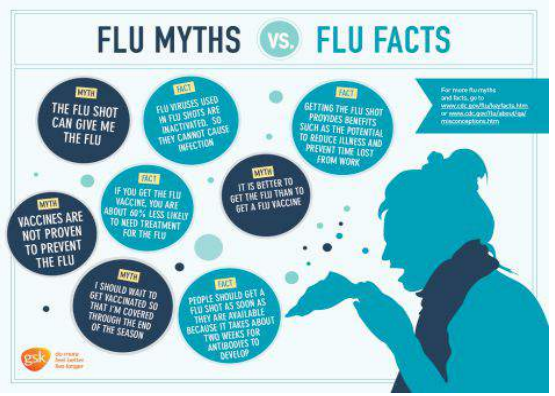
- Ventilation to maintain ≥12 ACH
- Positive room air pressure in relation to the corridor
- Self-closing door on all room exits

Surfaces

- Daily wet-dusting of horizontal surfaces using cloths moistened with EPA-registered hospital disinfectant/detergent
- Avoid dusting methods that disperse dust
- No carpeting in patient rooms or hallways
- No upholstered furniture and furnishings

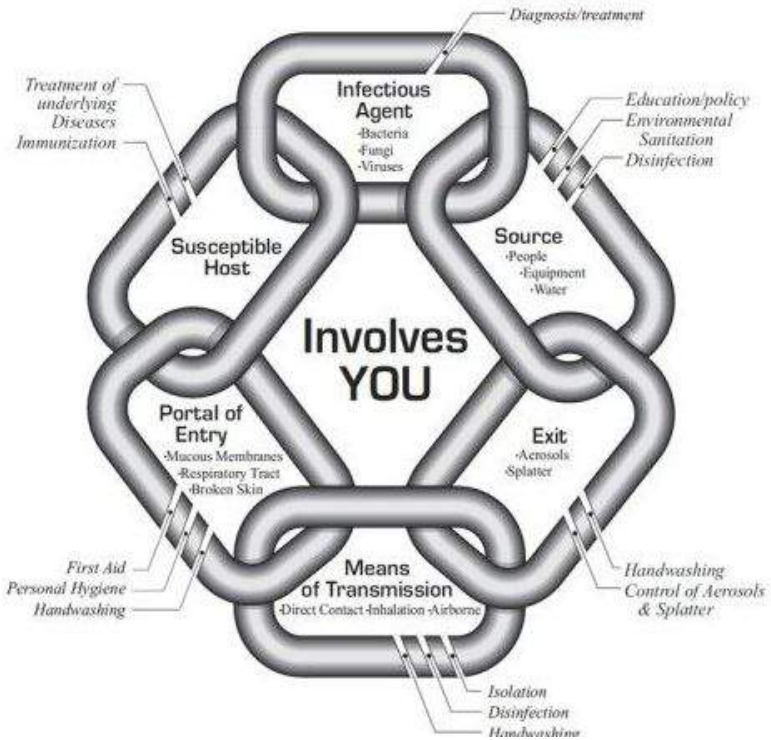
Other

- No flowers (fresh or dried) or potted plants in PE rooms or areas



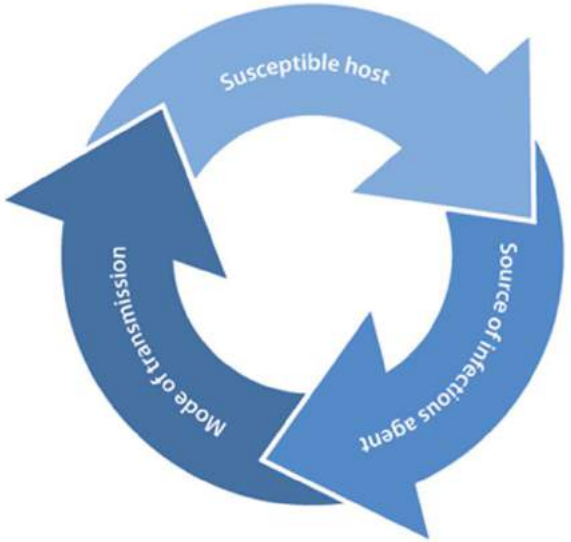
IMMUNIZATIONS

EVIDENCE BASED PRACTICE. SOURCES INFECTION



SOURCES OF INFECTION:

- People: Blood/body fluids, waste products (urine, faeces, vomit), respiratory discharges, skin.
- Equipment.
- Water.

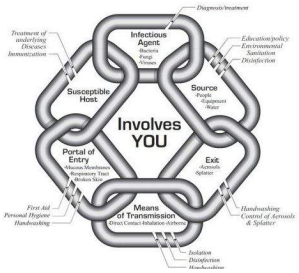


EVIDENCE BASED PRACTICE. MODE OF TRANSMISSION

Break the chain at the ‘mode of transmission’

Microorganisms are transmitted in health care settings by four main routes:

- Contact
- Droplet
- Airborne
- Common vehicle



Microorganisms vary by size, the length of time that they survive on surfaces or in the air and the method of getting around.
These factors plus the variability in virulence, the complications of treatment, and the complex symptoms, may require special treatment of some patients.

EVIDENCE BASED PRACTICE. MODE OF TRANSMISSION

CONTACT:

- Direct: involves direct body surface to body surface contact and physical transfer of microorganism between an infected or colonized person to another person by touch (skin to skin contact)

  Influenza virus, VRE; MRSA; C difficile

- Indirect: involves contact between a person and a contaminated object. This is often a result of unclean hands contaminating an object or environment. The microorganism remains on this surface to be picked up by the next person who touches it. (e.g., door handles, patient-care instruments or equipment, bed rails, pen, examination table).

  RSV; rhinovirus; norovirus

EVIDENCE BASED PRACTICE. MODE OF TRANSMISSION

DROPLETS:

- Via coughing or sneezing, or during suctioning.
- Droplets are relatively large (>5 µm) and can be projected up to about one metre these microorganisms land on another person, these infected droplets may linger on surfaces for long periods of time, so these surfaces (within the range of the coughing/sneezing person) will need additional cleaning.

  Influenza, colds, respiratory syncytial virus (RSV) and some organisms causing pneumonia.

AIRBORNE:

- Airborne droplet nuclei (small particles of 5 µm)
- Dust particles containing infectious agents.

Microorganisms carried in this manner remain suspended in the air for long periods of time and can be dispersed widely by air currents. Because of this, there is risk that all the air in a room may be contaminated.

M. tuberculosis, rubeola, varicella and hantaviruses.

EVIDENCE BASED PRACTICE. MODE OF TRANSMISSION

COMMON VEHICLE:

Applies to microorganisms that are transmitted by contaminated items such as food, water, medications, medical devices and equipment.

To inhibit the transmission of microorganisms by this mode:

- Clean patient equipment between uses with different patients (alcohol based chlorhexidine..) Local strategy.
- Handle, store and prepare food properly.
- Water care.
- Careful store and draw up doses of medication from multidose medication vials.

Assess infection hazards and risks and ensure that, where possible, infection risks are eliminated, reduced, contained and managed appropriately.

EVIDENCE BASED PRACTICE. DPI

PERSONAL PROTECTIVE EQUIPMENT:

- Gloves – protect hands
- Gowns/aprons – protect skin and/or clothing
- Masks and respirators– protect mouth/nose
- Goggles – protect eyes
- Face shields – protect face, mouth, nose, and eyes

The sequence for donning equipment

- Gown first
- Mask or respirator
- Goggles or face shield
- Gloves

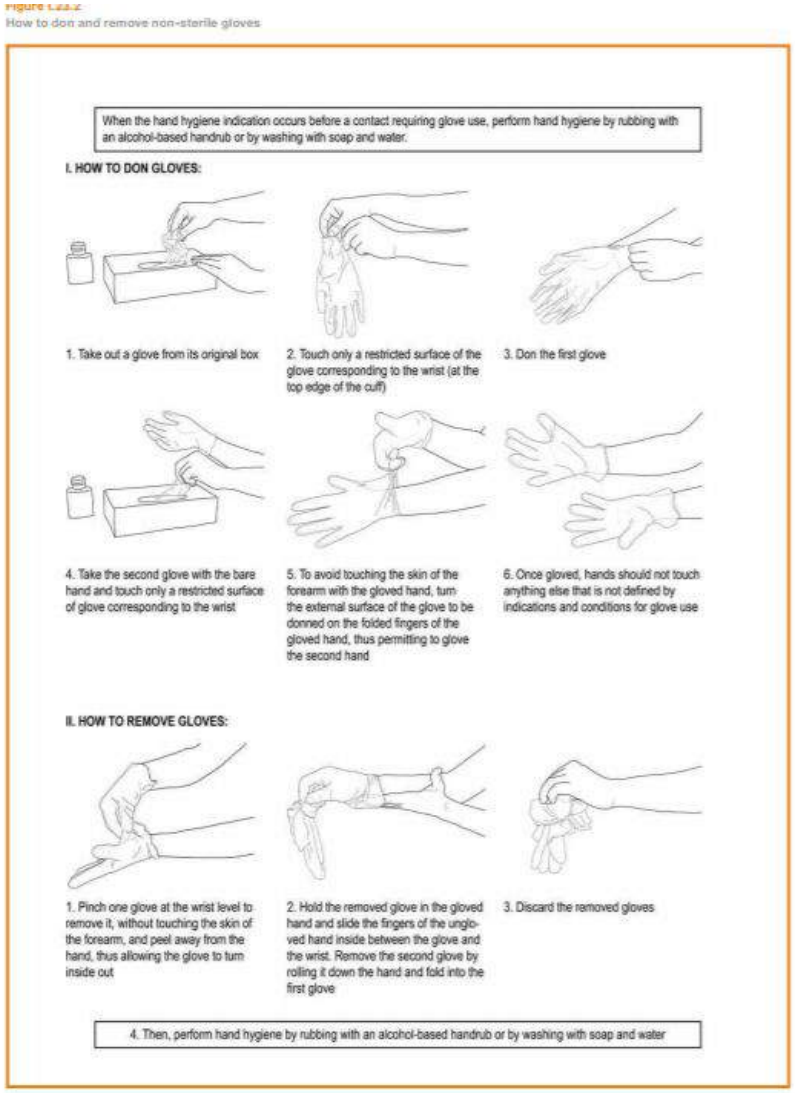
The sequence for removing equipment:

- Gloves
- Goggles or face shield
- Gown
- Mask or respirator

To limit opportunities for self-contamination. Gloves are the most contaminated piece.

EVIDENCE BASED PRACTICE. HAND HYGIENE

GLOVE USE DOES NOT modify hand hygiene indications or REPLACE hand hygiene by washing with soap and water or handrubbing with an alcohol-based handrub.
Gloves represent a risk for pathogen transmission and infection if used inappropriately.



EVIDENCE BASED PRACTICE. HAND HYGIENE

Hands are the most common vehicle of transmission of organisms

HAND HYGIENE has been recognized as the single most important way to prevent the transmission of infectious agents.

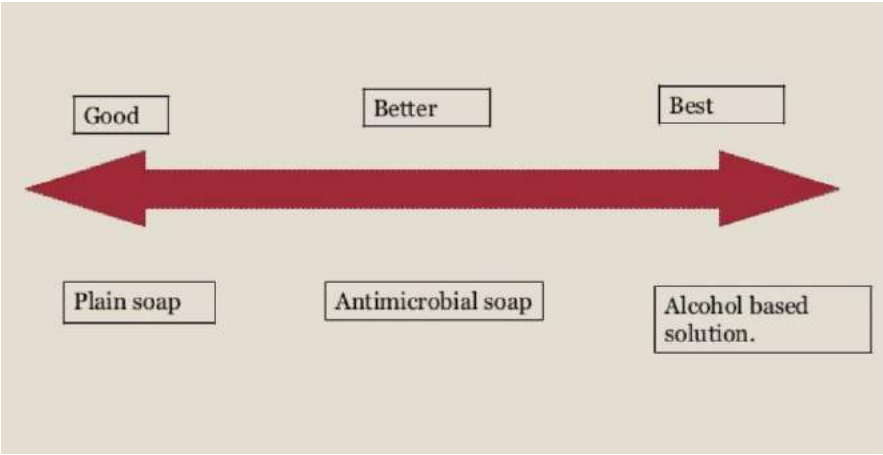
EVIDENCE BASED PRACTICE. HAND HYGIENE

Table I.11.7
Antimicrobial activity and summary of properties of antiseptics used in hand hygiene

Antiseptics	Gram-positive bacteria	Gram-negative bacteria	Viruses enveloped	Viruses non-enveloped	Myco-bacteria	Fungi	Spores
Alcohols	+++	+++	+++	++	+++	+++	-
Chloroxylenol	+++	+	+	±	+	+	-
Chlorhexidine	+++	++	++	+	+	+	-
Hexachlorophene[a]	+++	+	?	?	+	+	-
Iodophors	+++	+++	++	++	++	++	±[b]
Triclosan[d]	+++	++	?	?	±	±[e]	-
Quaternary ammonium compounds[c]	++	+	+	?	±	±	-

Antiseptics	Typical conc. in %	Speed of action	Residual activity	Use
Alcohols	60-70 %	Fast	No	HR
Chloroxylenol	0.5-4 %	Slow	Contradictory	HW
Chlorhexidine	0.5-4%	Intermediate	Yes	HR,HW
Hexachlorophene[a]	3%	Slow	Yes	HW, but not recommended
Iodophors	0.5-10 %)	Intermediate	Contradictory	HW
Triclosan[d]	(0.1-2%)	Intermediate	Yes	HW; seldom
Quaternary ammonium compounds[c]		Slow	No	HR,HW; Seldom; +alcohols

Good = +++, moderate = ++, poor = +, variable = ±, none = –
HR: handrubbing; HW: handwashing
*Activity varies with concentration.
[a] Bacteriostatic.
[b] In concentrations used in antiseptics, iodophors are not sporicidal.
[c] Bacteriostatic, fungistatic, microbicidal at high concentrations.
[d] Mostly bacteriostatic.
[e] Activity against *Candida* spp., but little activity against filementous fungi.
Source: adapted with permission from Pittet, Allegranzi & Sax, 2007.[479]



EVIDENCE BASED PRACTICE. HAND HYGIENE

World Health Organization | Patient Safety — A World Alliance for Safer Health Care | SAVE LIVES Clean Your Hands

At present, alcohol-based handrubs are the only known means for rapidly and effectively inactivating a wide array of potentially harmful microorganisms on hands.

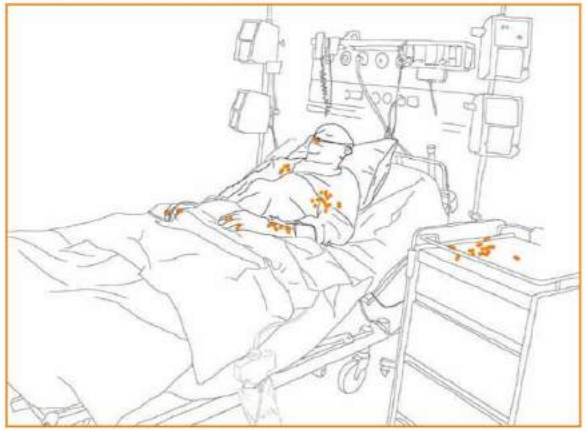
WHO recommends alcohol-based handrubs based on the following factors:

1. **evidence-based**, intrinsic advantages of **fast-acting and broad-spectrum** microbicidal activity with a minimal risk of generating resistance to antimicrobial agents
2. suitability for use in **resource-limited or remote areas** with lack of accessibility to sinks or other facilities for hand hygiene (including clean water, towels, etc.)
3. capacity to promote improved **compliance** with hand hygiene by making the **process faster** and more convenient
4. **economic benefit** by reducing annual costs for hand hygiene
5. **minimization of risks from adverse events** because of increased safety associated with better acceptability and tolerance than other products

<u>For optimal compliance with hand hygiene, handrubs should be readily available, either through dispensers close to the point of care or in small bottles for on-person carriage.</u>

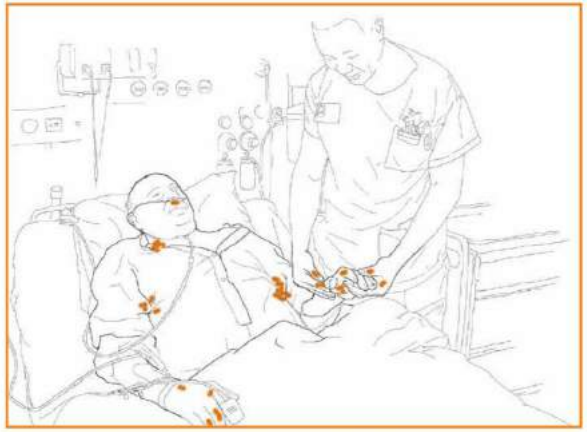
EVIDENCE BASED PRACTICE. HAND HYGIENE

Figure I.7.1
Organisms present on patient skin or the immediate environment



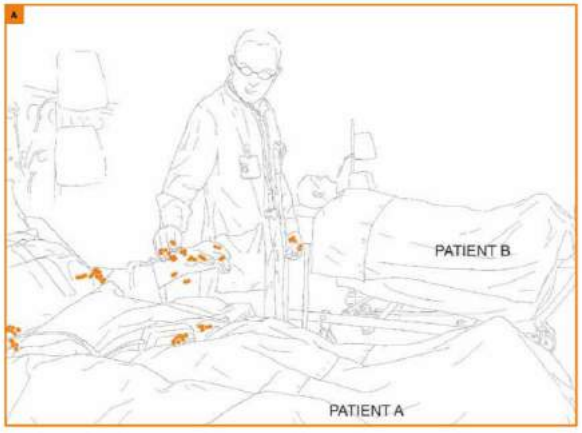
A bedridden patient colonized with Gram-positive cocci, in particular at nasal, perineal, and inguinal areas (not shown), as well as axillae and upper extremities. Some environmental surfaces close to the patient are contaminated with Gram-positive cocci, presumably shed by the patient. Reprinted from Pittet, 2000[488] with permission from Elsevier.

Figure I.7.2
Organism transfer from patient to HCWs' hands



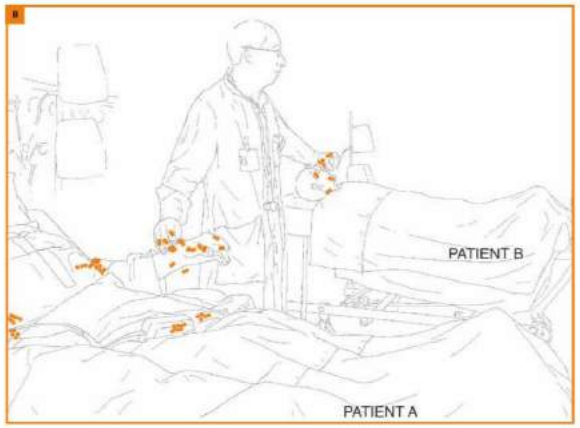
Contact between the HCW and the patient results in cross-transmission of microorganisms. In this case, Gram-positive cocci from the patient's own flora transfer to HCW's hands. Reprinted from Pittet, 2000[488] with permission from Elsevier.

Failure to cleanse hands results in between-patient cross-transmission*



(A) The doctor had a prolonged contact with patient A colonized with Gram-positive cocci and contaminated his hands. Reprinted from Pittet, 2000[488] with permission from Elsevier.
* The figure intentionally shows that long-sleeved white coats may become contaminated by microorganisms during patient care. Although evidence to formulate it as a recommendation is limited, long sleeves should be avoided.

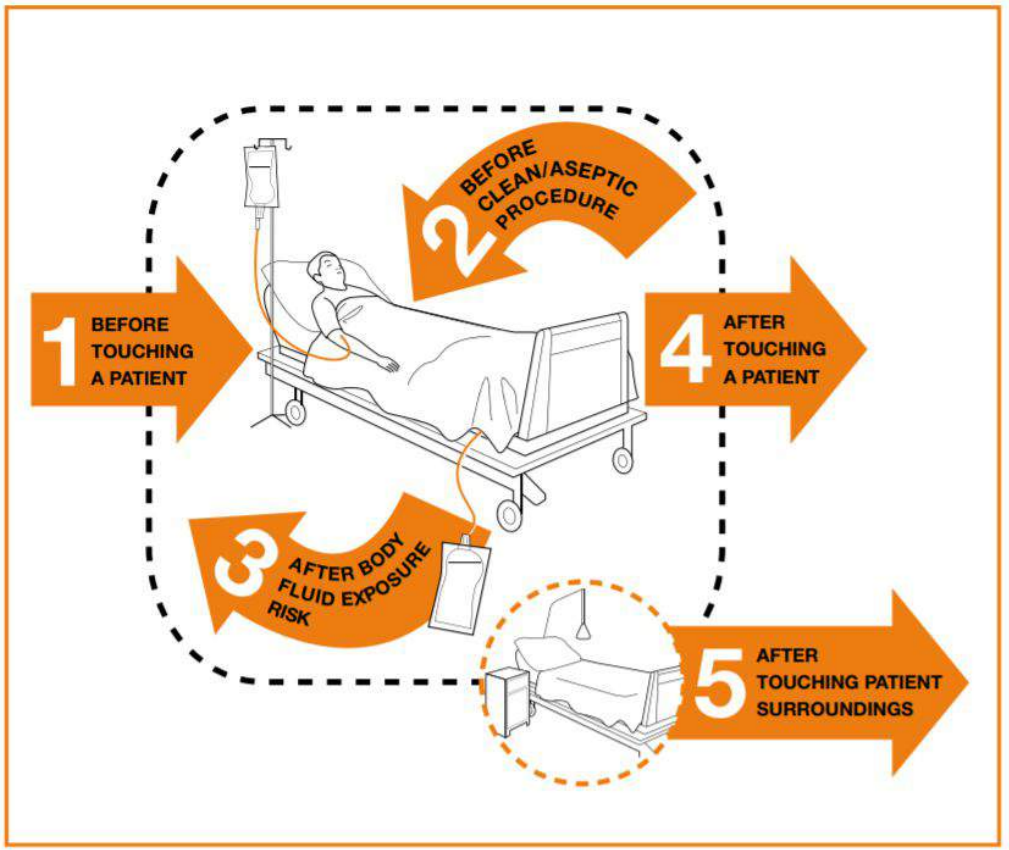
Figure I.7.3b
Failure to cleanse hands results in between-patient cross-transmission*



(B) The doctor is now going to have direct contact with patient B without cleansing his hands in between. Cross-transmission of Gram-positive cocci from patient A to patient B through the HCW's hands is likely to occur. Reprinted from Pittet, 2000[488] with permission from Elsevier.
* The figure intentionally shows that long-sleeved white coats may become contaminated by microorganisms during patient care. Although evidence to formulate it as a recommendation is limited, long sleeves should be avoided.

EVIDENCE BASED PRACTICE. PRECAUTIONS

Figure I.21.5b
Unified visuals for "My five moments for hand hygiene"



The *patient zone*, *health-care area*, and *critical sites* with inserted time-space representation of "My five moments for hand hygiene" (Figure I.21.5b).
Reprinted from Sax, 2007[1] with permission from Elsevier.

EVIDENCE BASED PRACTICE. HAND HYGIENE

EVIDENCE BASED PRACTICE. HAND HYGIENE

Figure II.2
How to handwash

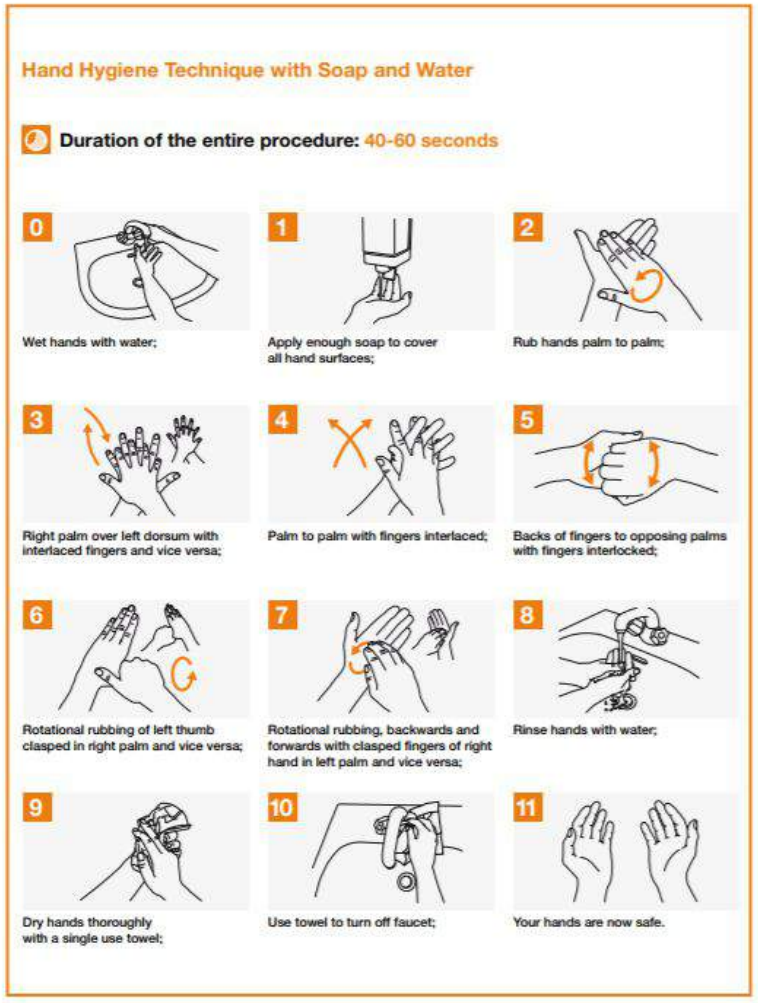
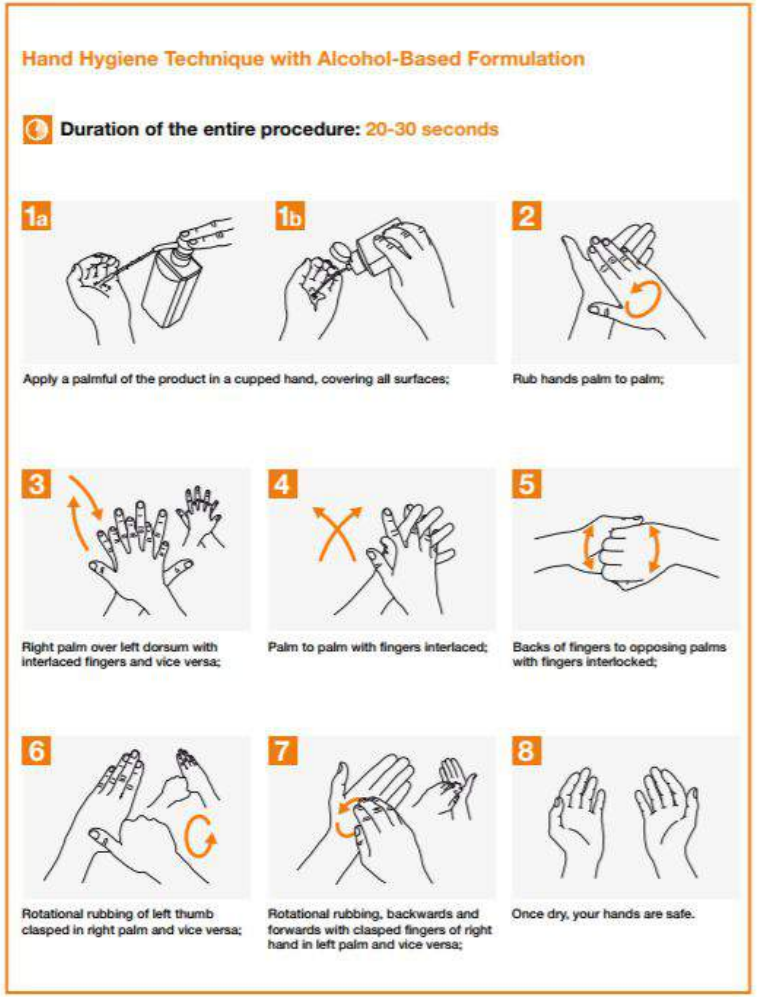


Figure II.1
How to handrub



EVIDENCE BASED PRACTICE. HAND HYGIENE

Poor adherence:

- Handwashing agents cause irritation and dryness
- Sinks are inconveniently located/lack of sinks
- Lack of soap and paper towels
- Too busy / insufficient time
- Understaffing/overcrowding
- Patient needs take priority
- Low risk of acquiring infection from patients

EVIDENCE BASED PRACTICE. HAND HYGIENE. Empower patients

Nurses Frontiers
www.edu-nursesnofrontiers.com
moodle

EBMT
European Society
for Blood and Marrow Transplantation

Respondents were asked to provide additional information relating to their experiences. Figure 2 illustrates some themes from around the world relating to patient-perceived barriers to involvement.

Figure 2.
Free text related to patient-perceived barriers to patient involvement

CONCLUSION

- Protective isolation is recommended for transplanted patients: Transplant process
- Be aware of the mode of transmissions that can lead to infections
- Education from Infection Control teams
- Education on handwashing. Training.
- Surveillance
- Monitoring outbreaks
- Audits

Protect your patients, protect your colleagues and protect yourself!

LITERATURE REFERENCE

- World Health Organization. Patient safety.
- CDC.Appendix A: Table 5. Components of a Protective Environment.
- JACIE standards 7th Edition.
- Protective environment for hematopoietic cell transplant (HSCT) recipients: The Infectious Diseases Working Party EBMT analysis of global recommendations on health-care facilities. Jan Styczynski et al.
- EBMT Handbook. Haematopoietic Stem Transplantation. Springer

Administration preparative regimens

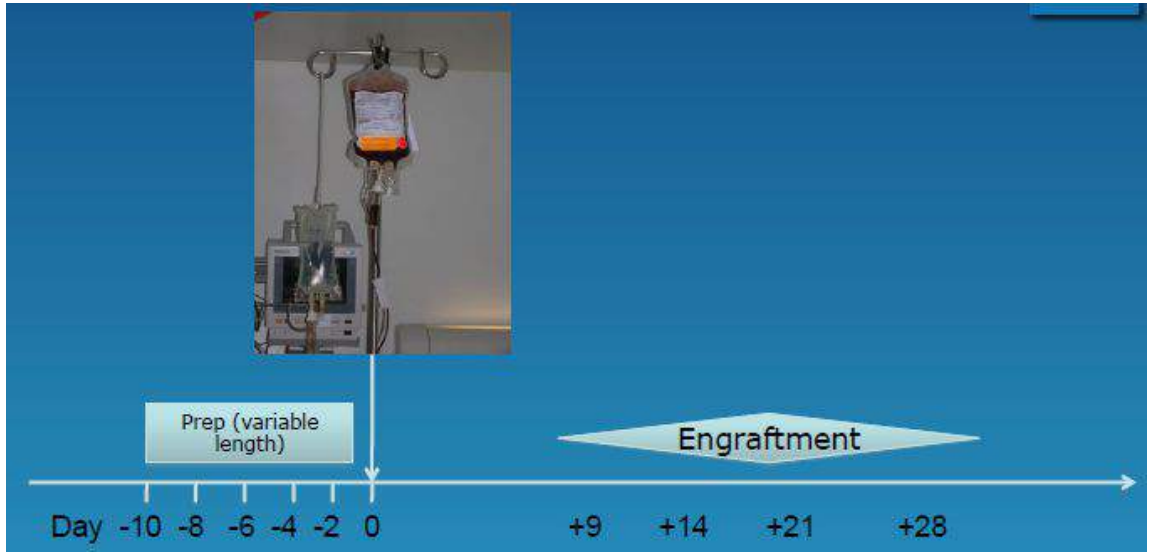
Julia Ruiz, Spain

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

INTRODUCTION. CONDITIONING

- Prepare patient for transplant
- Inpatient or outpatient setting
- Conditioning therapy:
  - Single or multiple chemotherapy
  - Radiation therapy (TBI)
  - Immunotherapy
- In general: 4 to 10 days depending on the disease and type of transplant.
- Immunosupresive drugs



INTRODUCTION. CONDITIONING JACIE

- Complex therapy
- Develope SOPs by a interdisciplinary team for preparing and administration of conditioning.

STANDARD:
B7.4 *There shall be a policy addressing safe administration of the preparative regimen.*

Explanation:
Preparative regimens encompass various modalities, such as biologic, radiologic, and chemotherapy. It is recommended that a tracking system regarding mixture, delivery, and completed administration be instituted for all regimens based upon these drugs. Staff administering the preparative regimen shall be appropriately credentialed as defined by institutional policies and in accordance with governmental laws and regulations.

B7.4.1 The treatment orders shall include the patient's current height and weight, specific dates of administration, daily doses (if appropriate), and route of administration of each agent.

STANDARD:
B7.4.2 *Preprinted orders or electronic equivalent shall be used for protocols and standardized regimens. These orders shall be verified and documented by an attending physician.*

EVIDENCE BASED PRACTICE. JACIE

CLOSE COOPERATION:

PHARMACIST

TRANSPLANT TEAM

"4 eyes" principle

CHECK POINTS:

Right patient

Right drug

Correct dose

Appropiate timing

***Pediatric patients: prescriptions are done by body surface area, using weight and height.**

STANDARD:

B7.4.3 *The pharmacist verifying or preparing the drug shall check and document the doses against the protocol or standardized regimen listed on the orders.*

B7.4.4 *Prior to administration of the preparative regimen, one (1) qualified person using a validated process or two (2) qualified persons shall verify and document:*

B7.4.4.1 *The drug and dose in the bag or pill against the orders and the protocol or standardized regimen.*

B7.4.4.2 *The identity of the recipient.*

EVIDENCE BASED PRACTICE. NURSE ASSESMENT

- Nurses: Update knowledge, training, and demonstrated competency.
- Develope policies and procedures for administration of chemotherapy with the interdisciplinary team.
- Nurses are on the forefront of care delivery:
  - Recognize problems
  - Education: Patient and caregiver on the purpose of the preparative regimen:
    - Name, dose, schedule and side effects of each chemotherapy agent, long term side effects
    - TBI schedule, short and long term side effects
    - Differences between conditioning and previous chemotherapy treatments
    - Develope written material: Patient education handbook.
  - Pediatric:
    - Tolerate side effects better.
    - Conditioning affects growth and endocrine development: Retarded growth and failed or retarded puberty are main late effects.

EVIDENCE BASED PRACTICE. NURSE MANAGEMENT

- Recognize, prevent and treat expected and unexpected toxicities caused by chemotherapy and TBI.
  - Nausea and vomiting
    - Antiemetics
  - Bladder toxic drugs
    - Hydratation
  - Nephrotoxic agents:
    - Daily weight
    - Patient´s intake and output monitoring

Table 6: **Agents used in the prevention of acute graft-versus-host disease**

Agent	Mechanism of action	Dose
Cyclosporin	Calcineurin inhibition i.e. blockade of T-cell activation	3 mg/kg iv
Tacrolimus	Calcineurin inhibition i.e. blockade of T-cell activation	0.02 mg/kg iv
Methotrexate	Antimetabolite	15 mg/m² day +1, 10 mg/m² day +3, 6 and 11
Methylprednisolone	Receptor mediated lympholysis and other unidentified actions	0.5–1.0 mg/kg
Mycophenolate mofetil	Inhibition of DNA synthesis, lymphocyte apoptosis	1.5–3 g/day
Sirolimus	Macrolide antibiotic; blockade of T-and B-cell activations	12 mg day -3 then 4 mg/day
Antithymocyte globulin	Rabbit or equine polyclonal antibodies recognising T-cells	2.5 mg/kg/day x 4
Monoclonal antibodies eg. alemtuzumab (anti-CD52)	Humanised monoclonal antibodies recognising T-cells	10 mg/kg/day, usually for 5 days
Cyclophosphamide	Cytotoxic agent inducing death of proliferating cells	50 mg/kg/day on days +3 and +4

- Other supportive therapies: *prophilaxis*
  - Infections: Initiation of bacterial, viral and fungal prophylaxis
  - VOD: Veno-occlusive disease: evaluation of risk factors, prevention: sodium heparin, prostaglandin E1, ursodeoxycholic acid, low molecular weight heparine, defibrotide.
  - GVHD: prophylaxis directed towards immunosuppression of donor T-cell function through the peri- and post-transplant by administration of immunosuppressive agents

EVIDENCE BASED PRACTICE. NURSE MANAGEMENT

- Antithymocyte globulin (ATG) (an immune globulin): Fever, chills, rash, anaphylaxis. Premedication.
- Cyclosporine, used in combination with other immunosuppressive agents: High blood pressure, nausea and vomiting, renal function.
- Tacrolimus for unrelated and mismatched transplants because it has proven to be superior to cyclosporine in this group of patients.
- Monoclonal antibodies, such as alemtuzumab (Campath) and anti CD45 antibody, are being incorporated into conditioning regimens as GvHD prophylaxis. Fever and chills, nausea and vomiting, itching, skin rash, fatigue headache, diarrhea, shortness of breath, and/or low blood pressure. Premedication.
- T-cell depletion, monoclonal antibodies, and CD34 + selection are successful strategies to deplete alloreactive T-cells from donor grafts.

1. ALKYLATING AGENTS:

MELPHALAN, CYCLOPHOSPHAMIDE, IFOSFAMIDE, BUSULFAN

Causes intracellular alteration in transcription and replication of DNA.

- Myelosuppression
- Nausea, vomiting, anorexia
- Diarrhea, constipation
- Mucositis
- Alopecia
- Allergic and cutaneous reactions
- Elevated liver function tests
- Gastrointestinal toxicity
- Neurological toxicity

EVIDENCE BASED PRACTICE. NURSE MANAGEMENT

CYCLOPHOSPHAMIDE-IFOSFAMIDE:

Mild dysuria to severe hemorrhage: Hemorrhagic cystitis.

- Mesna is a bladder protectant administered to decrease effects

CYCLOPHOSPHAMIDE

- Slow infusion
- Encourage hydration and frequent voiding
- Administration of mesna
- Monitor specific gravity and heme before and during administration
- Highly emetic: provide antiemetics
- Skin irritant

IFOSFAMIDE

- Administration pre- and post-hydration with mesna
- Monitor specific gravity and heme before and during administration
- Skin irritant

EVIDENCE BASED PRACTICE. NURSE ASSESMENT

MELPHALAN

- Administer hydration
- Maintain adequate urinary output
- Skin irritant

THIOTEPA

- Skin irritant
- Bathe patients 3–4 times/day during and for 24 h after
- Infusion/avoid creams and lotions
- Change diapers frequently, change linens with each bath,
- Avoid occlusive dressings
- Avoid all skin contact

BUSULFAN

- Seizures: prophylaxis medication

TREOSULFAN

2. PLANT DERIVATIVES:

ETOPOSIDE

Podophyllotoxins Topoisomerase II inhibitors: act by interfering with the function of topoisomerase enzymes, which are responsible for DNA arrangement and rearrangement and cell growth and replication.

ETOPOSIDE

- Use non-PVC bag/tubing: etoposide can crack plastic
- Skin irritant, eye irritant
- Hypotension with rapid infusion: monitor blood pressure
- Risk for acute HSR

3. ANTIMETABOLITES:

Acts at cellular metabolism, making cells unable to divide.

CYTARABINE, FLUDARABINE

- Myelosuppression,
- Mucositis,
- Nausea, and vomiting,
- Alopecia

CYTARABINE

- Highly emetic: provide antiemetics
- Conjunctivitis with high dose: administer steroid eye drops
- Monitor liver function tests

FLUDARABINE

- Pulmonary function tests recommended prior, during, and after treatment

EVIDENCE BASED PRACTICE. NURSE ASSESMENT

Table 4-2. Side Effects of Preparative Regimens by Agent and System

System	Cyclophosphamide	Busulfan	Carboplatin	Thiotepa	Melphalan	Carmustine	Cytarabine	Etoposide	Fludarabine	Mitoxantrone	TBI
Hematopoietic											
Anemia	X	X	X	X	X	X	X	X	X	X	X
Leukopenia	X	X	X	X	X	X	X	X	X	X	X
Thrombocytopenia	X	X	X	X	X	X	X	X	X	X	X
Gastrointestinal											
Nausea/vomiting	X	X	X	X	X	X	X	X	X	X	X
Anorexia				X			X	X			
Mucositis/stomatitis	X	X	X	X	X		X	X	X	X	X
Diarrhea	X		X		X		X	X	X	X	X
Constipation			X						X		
Hepatotoxicity/HSOS	X	X		X		X	X	X			X
Genitourinary											
Hemorrhagic cystitis	X			X							
Nephrotoxicity	X		X	X		X			X		X
Electrolyte imbalances	X		X					X			
Cardiovascular											
Cardiotoxicity	X	X								X	X
Hypo- or hypertension		X						X			
Pulmonary											
Fibrosis	X	X			X	X		X			X
Pneumonitis	X	X				X		X	X	X	X
Reproduction											
Infertility	X	X		X	X	X					X

(Continued on next page)

EVIDENCE BASED PRACTICE. NURSE ASSESMENT

Table 4-2. Side Effects of Preparative Regimens by Agent and System *(Continued)*

System	Cyclophosphamide	Busulfan	Carboplatin	Thiotepa	Melphalan	Carmustine	Cytarabine	Etoposide	Fludarabine	Mitoxantrone	TBI
Integumentary											
Dermatitis			X	X	X		X	X	X	X	X
Hyperpigmentation		X			X	X		X			X
Alopecia	X	X	X	X	X	X	X	X	X	X	X
Erythema	X	X		X		X	X	X		X	X
Immunologic											
Fever/chills				X			X	X	X	X	
Hypersensitivity/allergic reaction/anaphylaxis		X	X	X	X		X	X	X		
Neurologic											
Ototoxicity			X								
Peripheral neuropathy			X		X			X	X		
Seizures		X				X				X	
Headache/altered mental status	X	X		X	X	X	X		X	X	
Miscellaneous											
Secondary malignancy	X	X	X	X	X	X		X			X
Cataracts		X									X
Nasal congestion	X										
Conjunctivitis	X	X				X	X			X	
Parotitis											X
Thyroid disorders											X

HSOS—hepatic sinusoidal obstruction syndrome; TBI—total body irradiation

Note. Based on information from Camp et al., 2007; Forman & Nakamura, 2011; Iwamoto et al., 2012; Majhail & Weisdorf, 2008; Polovich et al., 2009.

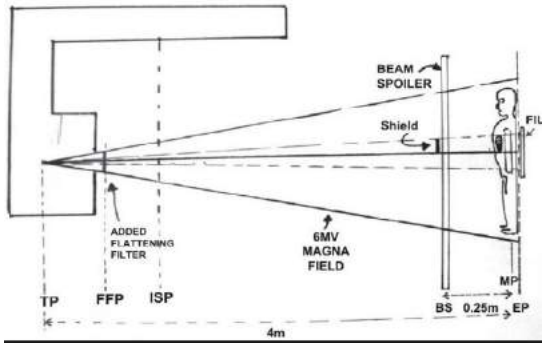
EVIDENCE BASED PRACTICE. NURSE ASSESMENT

TOTAL BODY IRRADIATION (TBI)

- Entire body with one dose of radiation or fractionated (minimises toxicity)
- Able to target sanctuary sites: central nervous system, gonads.

Side effects:

- Mild skin reaction
- Fatigue
- Acute toxicity: gastrointestinal toxicity, nausea, vomiting, mucositis.
- Long term effects: GVHD, cardiotoxicity, bronchiolitis obliterans, infertility, neurologic toxicity, cataracts
- TBI should be avoided in small children.



CONCLUSION

- Conditioning: Combination of chemotherapy, radiation and/or immunotherapy
- Critical issue: benefit of a quality management system.
  - SOPs describing: verification of conditioning regimen, administration
- Nurses:
  - Trained
  - Recognize problems
  - Prevent and treat toxicities
  - Provide education to patient, family.

LITERATURE REFERENCE

- ONS Hematopoietic Stem Cell Transplantation. Manual for nurse practice
- EBMT Handbook. Haematopoietic Stem Transplantation. Springer
- EBMT Textbook for Nurses. Springer
- Pediatric Oncology nursing. Springer
- JACIE standards 7th edition.

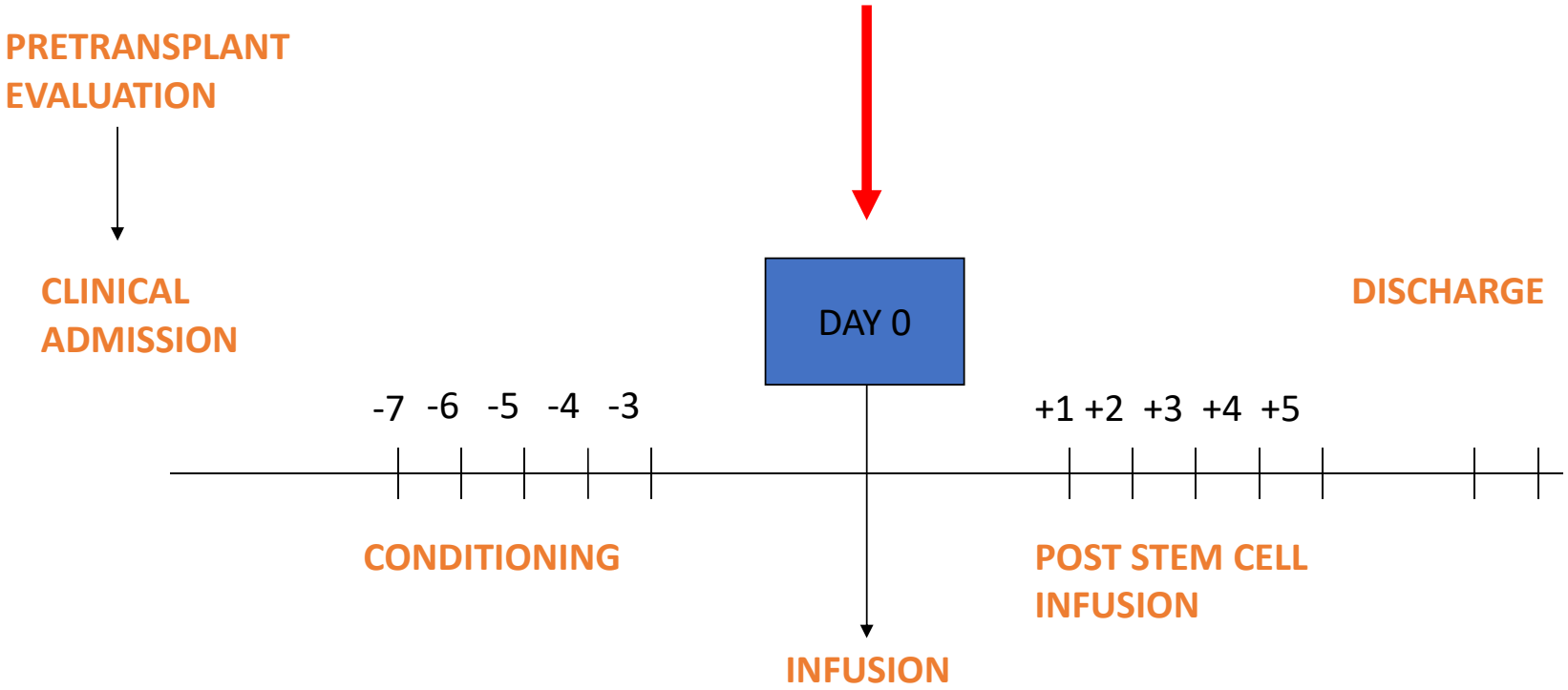
HPC product infusion and patient management

Julia Ruiz, Spain

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

INTRODUCTION. INFUSION HSC



AFTER DISCHARGE: CARE CONTINUES….LONG TERM CARE

INTRODUCTION. INFUSION HSC JACIE

HEMATOPOIETIC STEM CELLS:

- Patient: Autologous
  - Source:
    - Peripheral blood. Criopreserved
- Donor: Allogeneic
  - Source:
    - Peripheral blood: Criopreserved or fresh
    - Bone Marrow: Fresh (could be criopreserved)
    - Cord blood: Criopreseved

- Collection Unit: will provide HSC.
- Processing Laboratory: will process product
- Communication between Laboratory and Transplant Unit.
  - Who is the recipient?
  - Type of HSC?
  - Schedule time of infusion
  - Prepare patient for infusion

INTRODUCTION. INFUSION HSC JACIE

STANDARD:

B7.6 *There shall be policies addressing safe administration of cellular therapy products.*

Explanation:

Non-cryopreserved (often referred to as "fresh") cellular therapy products must be administered within the time specified by Clinical Program policies, registry and tissue bank requirements, and applicable laws and regulations. Thawed product administration should be completed as soon as possible. It may be optimal to thaw individual bags to reduce the time thawed products sit before administration.

Clinical Programs must identify appropriate timeframes between the end of the preparative regimen and administration of the cellular therapy product to confirm that the administered product is not affected by the preparative regimen. The program must verify that the preparative regimens were given at the scheduled time and delay administration of the cells if required. Programs are responsible for communicating with the Processing Facility regarding any delayed administration.

Clinical Programs need to determine the composition of the cellular therapy product to determine how it should be prepared for administration. Characteristics of the product, including the cell source (e.g., marrow, peripheral blood, cord blood), cell counts, etc. should be taken into consideration. Unless otherwise specified, the B7.6 standards apply to all products. Programs should work with their Processing Facilities to verify appropriate processing and preparation of the product for administration.

Evidence:

Staff should be prepared to discuss their normal practice and their training in the administration of cellular therapy products. Specific patient charts can be used to determine that two persons checked the product and that the documentation in the chart is complete. If there is time and an administration is scheduled on the day of inspection, the inspector should be notified so that he/she may watch parts of the procedure. If not, a mock procedure should be performed for inspector observation.

EVIDENCE BASED PRACTICE.
Nurse assessment HSC PRE-INFUSION

TRANSPLANT UNIT: Pre-infusion

- Room setup:
  - Access to patient
  - Monitoring equipment
  - Oxygen support and suction
  - **Emergency equipment**
- Education of patient and family
  - In general it is a safe procedure but there may be side effects: mild to severe reactions.
  - Discuss the procedure, offer reassurance to decrease patient anxiety.
  - Include what to expect before, during, after stem cell infusion: criopreserved product or fresh product.
- Baseline observations to assess patient´s physiological status: temperature, pulse, breathing rate, blood pressure, oxygen saturations.
- Check IV line for patency.

EVIDENCE BASED PRACTICE.
Nurse assessment HSC PRE-INFUSION

- Premedication:

  CRIOPRESERVED HSC:

  - *Antihistamine, corticosteroids, antipyretics and antiemetics.*
    - To reduce side effects of dimethylsulfoxide (DMSO) that is the cryoprotectant used in cells that are frozen and stored.
    - Hydratation (intravenous): may include sodium bicarbonate to alcalanize urine and prevent renal damage from any hemolyzed cells (breakdown of red cells)

  FRESH HSC:

  - *Antihistamine, antipyretics and antiemetics*
    - Hydratation (intravenous) including sodium bicarbonate to prevent renal damage: ABO incompatibility, hemolytic reaction.

PROCESSING LABORATORY

KEEP IN MIND: Unique product

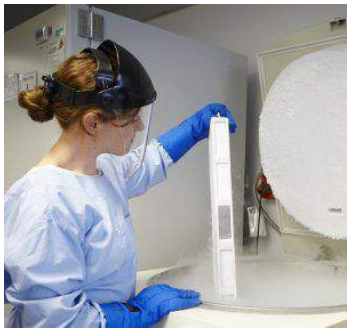
- Prepare the product
- Communicate with Transplant Unit
- Transport the product to the Trasplant Unit

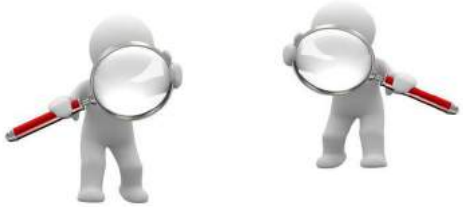
CRIOPRESERVED PRODUCT:

Frozen and stored at laboratory

HSC laboratory personnel after communication with transplant unit

- Prepare desinfected water bath: Heated sterile saline or sterile water 37ºC
- Remove the product (one at a time if several for infusion)
- Identification of product and recipient is verified by two trained staff members
- The product is introduced in a sterile bag to protect cells leakage, breakage
- Thawing: Immerse into the warm bath
- Ready for infusion





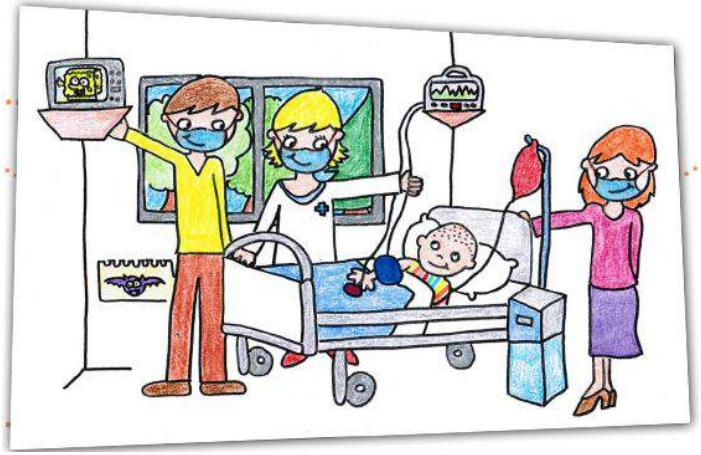
EVIDENCE BASED PRACTICE. PROCESSING LAB

FRESH PRODUCT:

Procesed at Laboratory:

- **Peripheral stem cell: Apheresis**
  - **Processing:**
    - Non manipulated
    - T-cell depletion: reduces incidence of GvHD
    - CD34+ selection
    - Other
  - Ready for infusion: communication with Transplant Unit
- **Marrow harvest:**
  - **Processing:**
    - Filtered to remove fat and bone particles
    - If recipient and donor have incompatible red cell phenotype the product will be red cell or plasma depleted.
  - Ready for infusion: communication with Transplant Unit

EVIDENCE BASED PRACTICE.
Nurse assessment HSC INFUSION



TRANSPLANT UNIT: Infusion

- Product transported from processing laboratory.
- Two trained staff members will check identification of product and patient.
- IV line: ensure aseptic non-touch technique
- Observation: patient´s physiological status, each 10-15 minutes vital signs
- <u>CRIOPRESERVED HSC:</u>
  - Infusion must start immediately if DMSO has not been removed, because the exposure of stem cells to DMSO decreases colony formation of cryopreserved HSC
- <u>FRESH HSC:</u>
  - Infusion via gravity (2-4 hours depending on volume)
  - ABO incompatibility?

B7.6.4 *Two (2) qualified persons shall verify the identity of the recipient and the product and the order for administration prior to the administration of the cellular therapy product.*

EVIDENCE BASED PRACTICE.
Nurse assessment HSC INFUSION

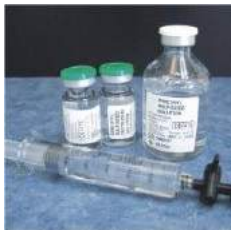
Adverse reactions and side effects.

Minor complications: 24-48 hours resolved

Treat side effects as they ocur, symptomatic treatment.

CRIOPRESERVED HSC:

- Bad taste in the mouth, nausea and vomiting caused by DMSO: hard candy or flavor ice pops.
- Flushing, rash, shortness of breath, fever, chills: antihistamine, antypiretics, oxigen
- Arrhythmia hypertensión: antihypertensive drugs
- Hemoglobinuria: Red urine caused by the breakdown of the red cells in the stem cell infusion product (24-36 hours): IV Hydratation and diuretics
- Fluid overload: Diuretics
- Hemolytic transfusion reaction
- Allergic reaction
- Anaphylactic reaction
- Others: tachypnea, chest tightness, hypotension, bradycardia, tachicardia



Adverse reactions and side effects.

Minor complications: 24-48 hours resolved

FRESH HSC:

Less adverse reactions.

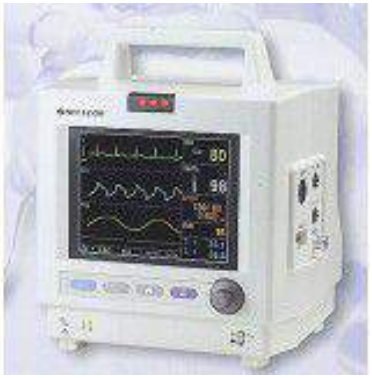
- Major risk associated with ABO incompatibility: Hemolytic transfusion reaction: symptomatic treatment, IV hydratation, diuretics.

  Similar to those with blood product infusions: shortness of breath, hypotension, hypertension, tachycardia, chills, fever, chest pain , flushing, nausea and vomiting, rash, hives or anaphylaxis.
- Fluid overload: diuretics
- Allergic reaction
- Anaphylactic reaction

Haploidentical transplant: Cytokine release síndrome (CRS) and neurologic toxicity (Immunotherapy)

EVIDENCE BASED PRACTICE.
Nurse assessment HSC INFUSION

PATIENT MANAGEMENT:



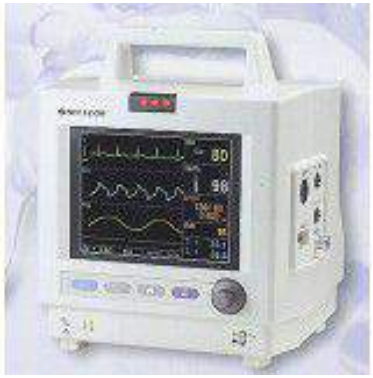
DMSO toxicity:

- Slow the rate of infusion as possible
- Administer symptomatic treatment: antihistamines
- Administer oxygen
- Monitor vital signs, oxygen saturation
- IV hydratation and diuretics if neccesary to prevent fluid overload

ABO incompatibility: hemolytic reaction

- Slow the rate of infusion
- Administer symptomatic treatment: hydrocortisone, antihistamines, epinephrine
- Administer oxygen
- Monitor vital signs, oxygen saturation
- IV hydratation and diuretics

EVIDENCE BASED PRACTICE.
Nurse assessment HSC INFUSION



PATIENT MANAGEMENT:

SEVERE REACTIONS:

ALLERGIC REACTION

ANAPHYLACTIC REACTION

- Follow centre guidelines for anaphylaxis event.
- Stop infusion if convenient following own procedures.
- Emergency equipment at bedside for cardiorespiratory support if needed.
- Posible ICU admission

EVIDENCE BASED PRACTICE. POST-HSC INFUSION

TRANSPLANT UNIT: Post Infusion

- Assess for late effects of the cell infusion.
- Observations: every half hour during 2 hours, hourly for 2 hours, and four hourly thereafter.
- Documentation: Document in patients´medical record: event and cell infusion.

STANDARD:

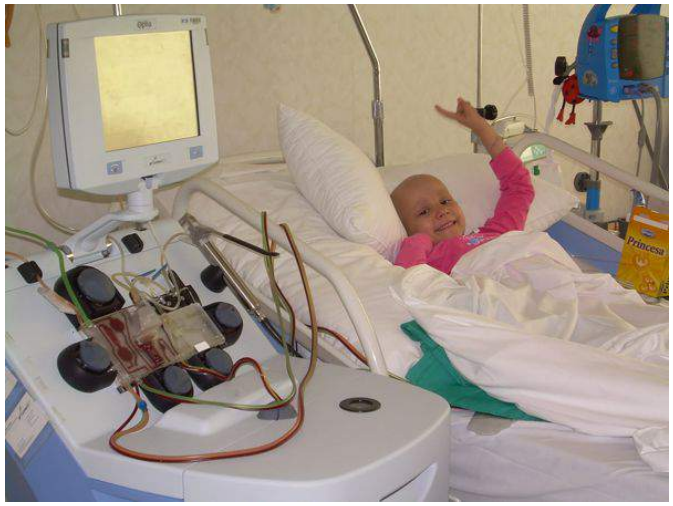
B7.6.6 *There shall be documentation in the recipient's medical record of the unique identifier of the administered cellular therapy product, initiation and completion times of administration, and any adverse events related to administration.*

DISCUSSION.
HSC POST-INFUSION

Relief when infusion has taken place.

Feeling of having reached a goal.

Make sure they have received all the information about transplant process, and the phases after cell infusion.



CONCLUSION

- Critical issue: benefit of a quality management system.
  - SOPs describing administration of HSC
- Stem cell infusion is a safe procedure.
- Although patient can have mild to severe reactions.
- Hematopoietic stem cell product may be a fresh or cryopreserved producto.
- Cryopreserved products have more adverse reactions caused by DMSO.
- Neccesary good communication between Proccessing Unit and Transplant Unit to schedule time of infusion
- Nurses:
  - Trained
  - Prevent side effects
  - Recognize side effects and adverse reactions
  - Provide education to patient, family.

LITERATURE REFERENCE

- ONS Hematopoietic Stem Cell Transplantation. Manual for nurse practice
- EBMT Handbook. Haematopoietic Stem Transplantation. Springer
- EBMT Textbook for Nurses. Springer
- Pediatric Oncology nursing. Springer

CELLULAR THERAPY

Julia Ruiz, Spain

Nurses No Frontiers - Training course for HSCT nurses – India

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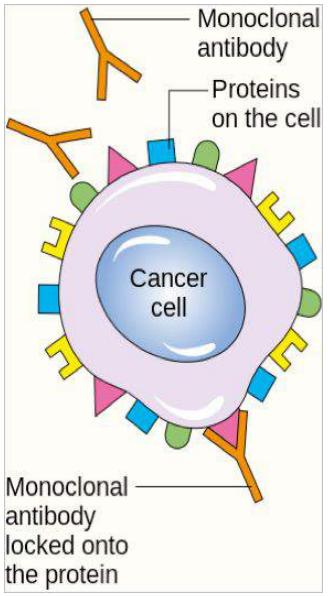
IMMUNOTHERAPY:

Treatment designed to harness body´s natural defences to fight cancer by improving or restoring immune system function

- Monoclonal antibodies
- T-cell therapy
- Non-specific immunotherapies
- Oncolytic virus therapy
- Cancer vaccines

INDICATION. Mab

MONOCLONAL ANTIBODIES

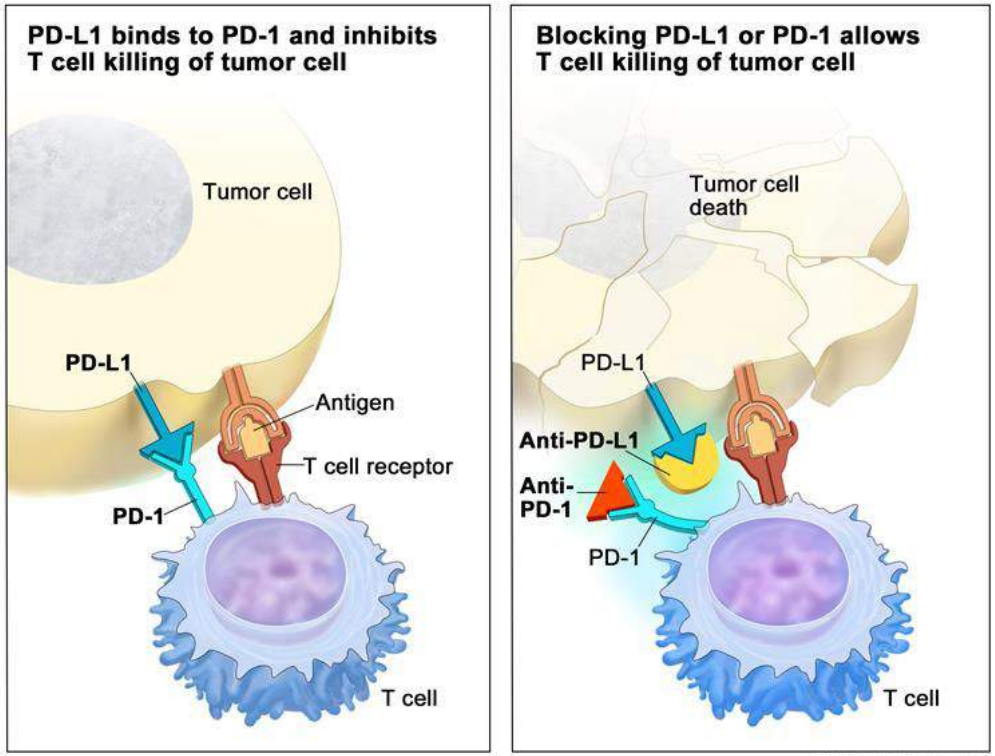


- Targeted therapy:
  - Bind to and inhibit the function of proteins expresed by cancer cells:
  - Destroying cells or slowing growth
  - Alemtuzumab (CD52), rituximab (CD20)

- Immune checkpoint blockade:
  - These inhibitors work by blocking pathways called checkpoints.
  - These checkpoint pathways are mechanisms for the human immune system to control the immune response.
  - These pathways can be co-opted to help cancer cells to evade cytotoxic T-cell–mediated death. ICPs work by preventing the receptors and ligands from binding to each other.
  - Ipilimumab, Nivolumab

INDICATION. Mab

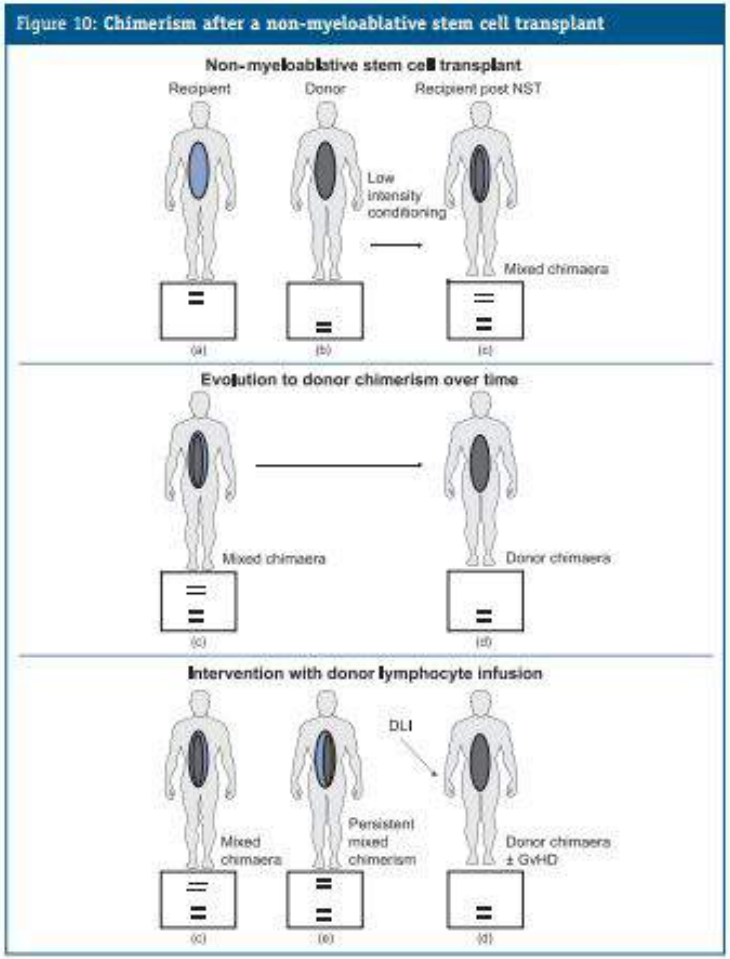
Immune checkpoint inhibitor. Checkpoint proteins, such as PD-L1 on tumor cells and PD-1 on T cells, help keep immune responses in check. The binding of PD-L1 to PD-1 keeps T cells from killing tumor cells in the body (left panel). Blocking the binding of PD-L1 to PD-1 with an immune checkpoint inhibitor (anti-PD-L1 or anti-PD-1) allows the T cells to kill tumor cells (right panel).



INDICATION. DLI

DONOR LYMPHOCYTE INFUSION

- T-cells are responsible for acute and chronic GvHD and for GvL effects.
- T-cell depletion of the stem cells prior to infusion is highly effective in the prevention of acute and chronic GvHD, but increases risk of graft rejection and disease relapse
- The concept of reduced intensity conditioning was introduced after studies that indicated:
  - the minimal requirements for stable engraftment
  - the capacity of donor lymphocyte infusion (DLI) to shift the balance between donor and recipient (chimerism) in a predictable way



Shows recipient (a) and donor (b) STR profiles prior to NST. Following reduced intensity conditioning a mixed chimaeric state is common (c). Overtime, this may progress to full donor chimerism (d). Persistent mixed chimerism is an indication for DLI (e) to convert the patient to a full donor chimaera (d)

INDICATION. DLI

OBJECTIVE:

- Increase the graft-versus leukemia response to treat or prevent disease relapse.
- Maximaze GVL and minimize toxicity (GVHD)
- Maximize donor chimerism and treat graft rejection
- Treat serious viral infections in the post SCT setting

*Haploidentical: DLI with GVHD prophylaxis, high rate of GVHD, response rates not clear.

DONOR:

Apheresis for collection

Criopreserved from the first collection

INFUSION:

Outpatient/Inpatient procedure

Usually cryopreserved product, so we must follow steps as described for infusion for cryopreserved products

INDICATION. DLI

FOLLOW-UP:

- Monitor chimerism
- Monitor the disease response
- Ensure the earliest identification and treatment of signs of GVHD

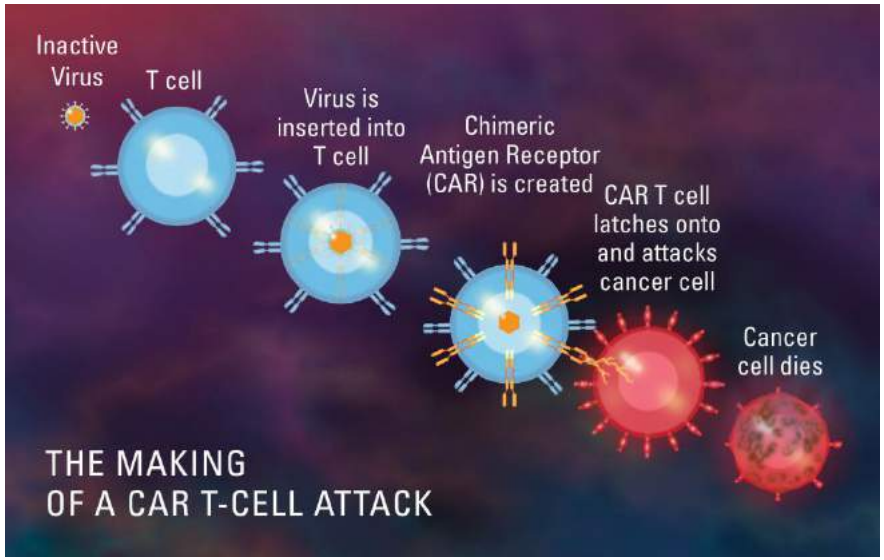
RESEARCH:

- Ongoing to find how to increase graft-versus-tumor effect and minimize or separate it from GVHD.
- Associated strageties:
  - DLI with targeted therapies in relapse
  - Conjunction with immunoregulatory agents
  - Manipulation of donor cells to be more tumor-specific: engineering donor T-cells and natural killer cells.

INDICATION. CAR-T

ADOPTIVE CELL THERAPY: CAR-T

- Chimaeric antigen receptor T-cell therapy: CAR-T
- T cells are collected from the blood
- Modified to express CAR protein
- Grown in laboratory
- Infused back to the patient.



EVIDENCE BASED PRACTICE. JACIE

STANDARD:

B7.11 *There shall be policies and Standard Operating Procedures addressing the administration of immune effector cells and management of complications, if applicable.*

B7.11.1 *There shall be a consultation with the referring physician prior to initiation of immune effector cellular therapy to review the goal and plan of the treatment.*

B7.11.2 *There shall be regular assessment of the recipient to detect complications, including cytokine release syndrome and neurologic dysfunction.*

B5.1.10 *Management of cytokine release syndrome and central nervous system toxicities.*

Explanation:

Cytokine release syndrome and central nervous system toxicities are adverse events that are common with the administration of immune effector cells, have been reported in haploidentical transplants, and are associated with antibodies such as Campath, Anti-thymocyte Globulin, and Rituximab. The Clinical Program must be aware of this and other nervous system issues resulting from these cellular therapy products.

CYTOKINE RELEASE SYNDROME

NEUROLOGIC TOXICITIES

EVIDENCE BASED PRACTICE. CRS

How I Treat

Current concepts in the diagnosis and management of cytokine release syndrome

Daniel W. Lee,[1] Rebecca Gardner,[2] David L. Porter,[3] Chrystal U. Louis,[4] Nabil Ahmed,[4] Michael Jensen,[2] Stephan A. Grupp,[3,5] and Crystal L. Mackall[1]

Risks associated with cancer immunotherapy can be broadly classified into autoimmune toxicity and cytokine-associated toxicity.

- **Autoimmune toxicity:** results from antigen-specific attack on host tissues when the targeted tumor associated antigen is expressed on nonmalignant tissue. Autoimmune toxicity occurs not uncommonly after treatment with checkpoint inhibitors
- **Cytokine release syndrome (CRS):** is a non–antigen-specific toxicity that occurs as a result of high-level immune activation

EVIDENCE BASED PRACTICE. CRS

CRS associated with:

- Monoclonal antibodies infusions: anti-CD3 (OKT3), anti-CD52 (alemtuzumab), anti-CD20 (rituximab) and Immune checkpoint inhibitors (Nivolumab)
- Infusion of haploidentical cells to patients with refractory leukemia
- Adoptive T cells engineered to express CARs

ONSET of symptoms and CRS severity:

- Depends on the inducing agent and the magnitude of immune cell activation.
- Rituximab for CD20 malignancies typically occurs within minutes to hours.
- Adoptive T-cell therapy:
  - Large tumor burdens leads to higher levels of T-cell activation with greater incidence and severity of the syndrome
  - Symptom onset typically occurs days to occasionally weeks after the T-cell infusion, coinciding with maximal in vivo T-cell expansion

EVIDENCE BASED PRACTICE. CRS- Haploidentical transplant

Highlights:

- Peripheral blood haploidentical hematopoietic cell transplant patients frequently develop signs and symptoms consistent with cytokine release syndrome (CRS)
- Some of these patients develop severe CRS needing aggressive supportive cares.
- Severe CRS is associated with poor survival and delayed neutrophil engraftment.
- Anti-IL6 (Tocilizumab) therapy is safe and well tolerated and may be an effective treatment for haplo-HCT related CRS.

Severe Cytokine Release Syndrome Following T-cell Replete Peripheral Blood Haploidentical Donor Transplant is Associated with Poor Survival and Anti-IL-6 Therapy is Safe and Well Tolerated

Ramzi Abboud[*,1], Jesse Keller[*,1], Michael Slade[*,1], John F. DiPersio[1], Peter Westervelt[1], Michael P. Rettig[1], Stephanie Meier[1], Todd A. Fehniger[1], Camille N. Abboud[1], Geoffrey L Uy[1], Ravi Vij[1], Kathryn M. Trinkaus[2], Mark A. Schroeder[1], and Rizwan Romee[1]

[1]BMT and Leukemia Program, Washington University School of Medicine, St Louis MO

[2]Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, Saint Louis, MO

Biol Blood Marrow Transplant. 2016 October ; 22(10): 1851–1860. doi:10.1016/j.bbmt.2016.06.010.

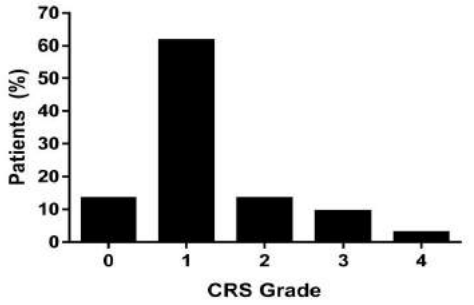


Figure 1A. Incidence of CRS by Severity in Haplo-HCT patients

EVIDENCE BASED PRACTICE.
CRS- grading and treatment

Table 1. Clinical signs and symptoms associated with CRS

Organ system	Symptoms
Constitutional	Fever ± rigors, malaise, fatigue, anorexia, myalgias, arthalgias, nausea, vomiting, headache
Skin	Rash
Gastrointestinal	Nausea, vomiting, diarrhea
Respiratory	Tachypnea, hypoxemia
Cardiovascular	Tachycardia, widened pulse pressure, hypotension, increased cardiac output (early), potentially diminished cardiac output (late)
Coagulation	Elevated D-dimer, hypofibrinogenemia ± bleeding
Renal	Azotemia
Hepatic	Transaminitis, hyperbilirubinemia
Neurologic	Headache, mental status changes, confusion, delirium, word finding difficulty or frank aphasia, hallucinations, tremor, dymetria, altered gait, seizures

Table 2. CRS revised grading system

Grade	Toxicity
Grade 1	Symptoms are not life threatening and require symptomatic treatment only, eg, fever, nausea, fatigue, headache, myalgias, malaise
Grade 2	Symptoms require and respond to moderate intervention Oxygen requirement <40% or Hypotension responsive to fluids or low dose[2] of one vasopressor or Grade 2 organ toxicity
Grade 3	Symptoms require and respond to aggressive intervention Oxygen requirement ≥40% or Hypotension requiring high dose* or multiple vasopressors or Grade 3 organ toxicity or grade 4 transaminitis
Grade 4	Life-threatening symptoms Requirement for ventilator support or Grade 4 organ toxicity (excluding transaminitis)
Grade 5	Death

Grades 2-4 refer to CTCAE v4.0 grading.
*High-dose vasopressor doses shown in Table 3.

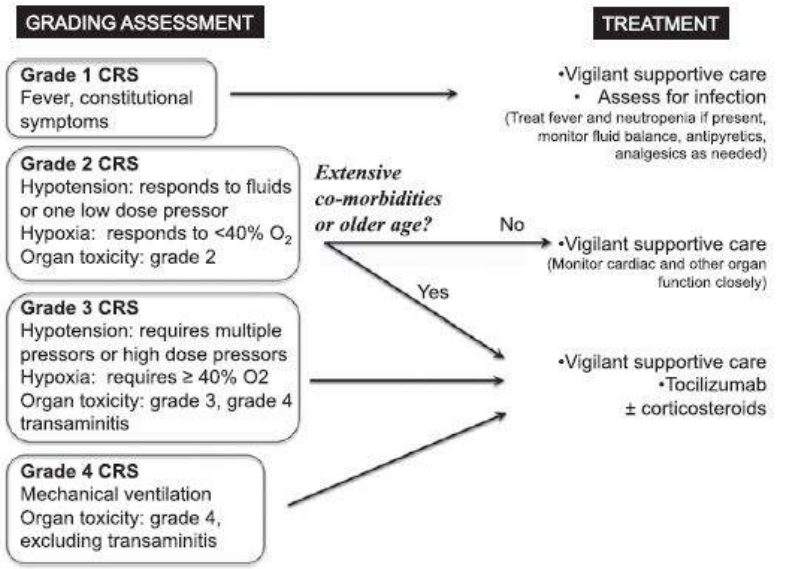


Figure 2. Treatment algorithm for management of CRS based on the revised CRS grading system. The algorithm uses the revised grading system for CRS to direct clinical management for patients with immunotherapy-associated CRS. We recommend vigilant supportive care including empiric treatment of concurrent bacterial infections and maintenance of adequate hydration and blood pressure for every grade. Immunosuppression should be used in all patients with grade 3 or 4 CRS and instituted earlier in patients with extensive comorbidities or older age. Grades 2-4 organ toxicities are dictated by CTCAE v4.0.

*If the patient's condition does not improve or stabilize within 24 hours of the tocilizumab dose, administration of a second dose of tocilizumab and/or a second immunosuppressive agent, such as corticosteroids, should be considered.

EVIDENCE BASED PRACTICE. CRS- Neurologic toxicity

- Neurologic symptoms associated with CRS sometimes follow a different time course of onset and resolution.
- In some patients hemodynamic instability resolves rapidly following administration of tocilizumab, but occasionally develop signs and symptoms of neurotoxicity.
- Cause: transit of IL-6 to CNS or activated immune cells to CNS (elevated IL-6 levels in the cerebrospinal fluid associated with neurotoxicity)
- Tocilizumab is not expected to cross the blood brain barrier.
- For patients with grade 3 or 4 CRS associated with neurologic dysfunction without significant hemodynamic instability or other lifethreatening symptomatology, consideration may be given to the use of corticosteroids as a preferred first-line immunosuppressive.

Other considerations:

- Once dexamethasone is initiated, give for a minimum of 3 doses or until resolution of CRS and any associated neurological symptoms
- Grade 1 : consider seizure prophylaxis (e.g. levetiracetam)
- Grade 2 : Frequent inpatient monitoring until fever and symptom resolution, include neurologic evaluations and symptomatic support (supplemental oxygen, IV fluids with aggressive electrolyte replacement, antipyretics, low-dose vasopressor support); initiate seizure prophylaxis (e.g. levetiracetam) and consider EEG monitoring if concurrent NT (see NT algorithm on Figure 2)
- Grade ≥3: ICU-level monitoring and symptomatic, hemodynamic, and respiratory support, include neurologic exams; initiate seizure prophylaxis (e.g. levetiracetam) and consider EEG monitoring if concurrent NT (see NT algorithm on Figure 2)

EVIDENCE BASED PRACTICE. CRS- Neurologic toxicity

Neurological toxicities associated with immune-checkpoint inhibitors

Mehdi Touat[a,b,c,d], Daniel Talmasov[e], Damien Ricard[c,f,g], and Dimitri Psimaras[a,b,c]

Curr Opin Neurol 2017, 30:000–000

Table 3. Selected neurologic immune-related adverse event involving the central and peripheral nervous system

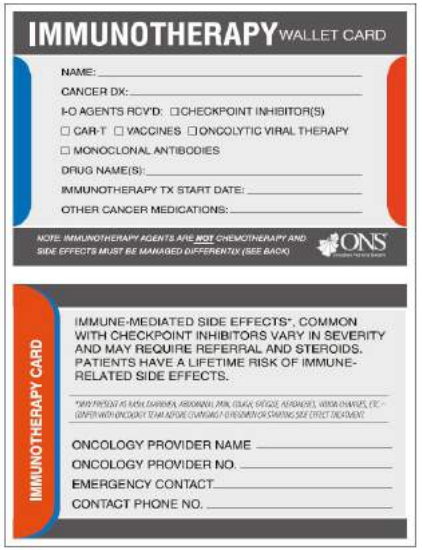
Type of irAE	Suspected causing agents	Estimated frequency (%)	Selected reported cases[a] (references)	Reported onset delay after ICI initiation (weeks)	Immune-modulating treatments	Reported outcome
irAE involving the central nervous system						
Encephalitis	Nivolumab, pembrolizumab, nivolumab + ipilimumab	0.1–0.2	8 [17▪,27–30]	4–28	Corticosteroids (7/8) IVIg (1/8)	Complete recovery (6/8) Partial improvement (1/8) Death (1/8)
Aseptic meningitis	Ipilimumab	NA	3 [33–35]	1–7	Corticosteroids (3/3)	Complete recovery (3/3)
irAE involving the peripheral nervous system						
Acute immune Demyelinating Polyneuropathy	Nivolumab, pembrolizumab, ipilimumab	0.1–0.2	4 [34,61–63]	5–12	Corticosteroids (4/4) IVIg (2/4) Plasmapheresis (1/4) Tacrolimus (1/4)	Complete recovery (2/4) Death (2/4)
Chronic immune Demyelinating Polyneuropathy	Nivolumab, pembrolizumab, nivolumab + ipilimumab	NA	5 [21,61,64–66]	1–44	Corticosteroids (4/5) IVIg (4/5) Plasmapheresis (3/5) Mycophenolate mophetil (1/5)	Partial recovery (4/5) NA (1/5)
Cranial nerves neuropathies	Pembrolizumab, ipilimumab	NA	4 [19,56–58]	0.5–16	Corticosteroids (4/4) Plasmapharesis (1/4)	Complete recovery (2/4) Partial recovery (2/4)
Myasthenic syndromes	Ipilimumab, nivolumab, pembrolizumab, nivolumab + ipilimumab	0.1–0.2	8 [21,37–39,41–43]	2–6	Corticosteroids (7/8) Plasmapheresis (5/8) IVIg (5/8)	Complete recovery (1/8) Partial recovery (3/8) Death (4/8)
Myositis	Ipilimumab, nivolumab, pembrolizumab, nivolumab + ipilimumab	0.1–0.2	7 [41,49–54]	2–8	Corticosteroids (7/7) Plasmapheresis (4/7) IVIg (2/7) Mycophenolate mophetil (1/7) Infliximab (1/7)	Complete recovery (3/7) Partial recovery (3/7) Death (1/7)

ICI, immune-checkpoint inhibitor; irAE, immune-related adverse event; IVIg, intravenous immunoglobulin; NA, data not available.
[a]Published case report/series with available clinical and paraclinical supporting drug-related neurological toxicity were selected.

EVIDENCE BASED PRACTICE. EDUCATION. Nurse assessment

VOLUME 36 · NUMBER 17 · JUNE 10, 2018
JOURNAL OF CLINICAL ONCOLOGY ASCO SPECIAL ARTICLE

Management of Immune-Related Adverse Events in Patients Treated With Immune Checkpoint Inhibitor Therapy: American Society of Clinical Oncology Clinical Practice Guideline



- Patients and family caregivers must receive timely and up-to-date education about immunotherapies, their mechanism of action, and the clinical profile of possible irAEs.
- Patient and caregiver education should occur prior to initiating therapy and continue throughout treatment and survivorship.
- Patients and caregivers need to know that AEs can often be managed effectively, especially when they are identified early.
- Health care professionals should ask patients about any new symptoms or changes in their health, no matter how small they may seem. Minor changes in how a patient is feeling may indicate early signs of an AE.

EVIDENCE BASED PRACTICE. Nurse assessment

Nurses must be trained:

CRS can range from mild response to severe

- Nursing recognition, assessment, and management is of utmost importance
- Symptoms can mimic sepsis or infection
- Can be present immediately to weeks after the infusion

NEUROLOGIC MANAGEMENT TOXICITIES

- May occur apart from CRS
- Signs and Symptoms include: Confusion, Somnolence, Tremors, Gait instability, Aphasia, other speaking difficulties, Seizures
- Give supportive care and antiepileptic

ORGAN DISFUNCTION. SEVERE CRS

EVIDENCE BASED PRACTICE.
Nurse assessment. Infusion

- Premedicate prior to infusion
- Vital signs pre-infusion, 15 minutes into infusion and then immediately after
- Neurological assessment every shift and on going (listen to the family)
- Look for new onset tremors, lethargy, slurred speech, expressive aphasia
- Intake and output every 8 hours
- Educate family if outpatient to call for any neurological concerns or fever

EVIDENCE BASED PRACTICE.
Nurse management CRS

- Control fever: Acetaminophen.
- Maintain oxygenation
- Maintain blood pressure
- Monitor lab values closely
- Monitor organ function
- Head to toe assessment:
    - look for capillary leak (lung sounds), or any other complaints
- CRS can mimic sepsis- think of differential diagnosis
- Prepare family and patient for possible ICU admission
- Support patient and family

CONCLUSION

- Cancer immunotherapy seeks to harness the power of the immune system to eradicate malignant tissues. Novel therapies.
- Risks associated with cancer immunotherapy: autoimmune toxicity and cytokine-associated toxicity.
- Develope SOPs describing administration of immune therapy and management of complications.
- Nurses trained:
  - To recognize the use of different immunotherapies
  - To recognize adverse events, CRS, neurological toxicity and onset.
  - Provide education to patient, family.

Literature reference

- Lee, D., Gadner, R., Porter, D., Louis., Ahmed, N., Jensen, M….Mackall, C. 92014). Current concepts in the diagnosis and management of cytockine release syndrome. *Blood Journal,* 118-195. doi10.1182/blood-2014-05-552729.
- Ramzi Abboud et al. Severe Cytokine Release Syndrome Following T-cell Replete Peripheral Blood Haploidentical Donor Transplant is Associated with Poor Survival and Anti-IL-6 Therapy is Safe and Well Tolerated. Biol Blood Marrow Transplant. 2016 October
- Jolenes-car-t-cell-therapy.
- EBMT Textbook for Nurses. Springer
- The EBMT handbook 2012.
- JACIE STANDARDS 7th Edition.

THANK YOU FOR YOUR ATTENTION.

Early and acute complications in BMT setting, diagnosis and management:

- Management of mucositis & oral care, nausea, vomiting and pain management
- Central venous access devices (care of CVAD: Hickman, port and PICC)
- Neutropenic fever, management of thrombocytopenia and bleeding

Alberto Castagna, Italy

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

Nurses Frontiers
www.edu-nursesnofrontiers.com
moodle

EBMT
European Society
for Blood and Marrow Transplantation

Early and acute complications in BMT setting, diagnosis and management:

No conflict of interest

Alberto Castagna, Italy

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

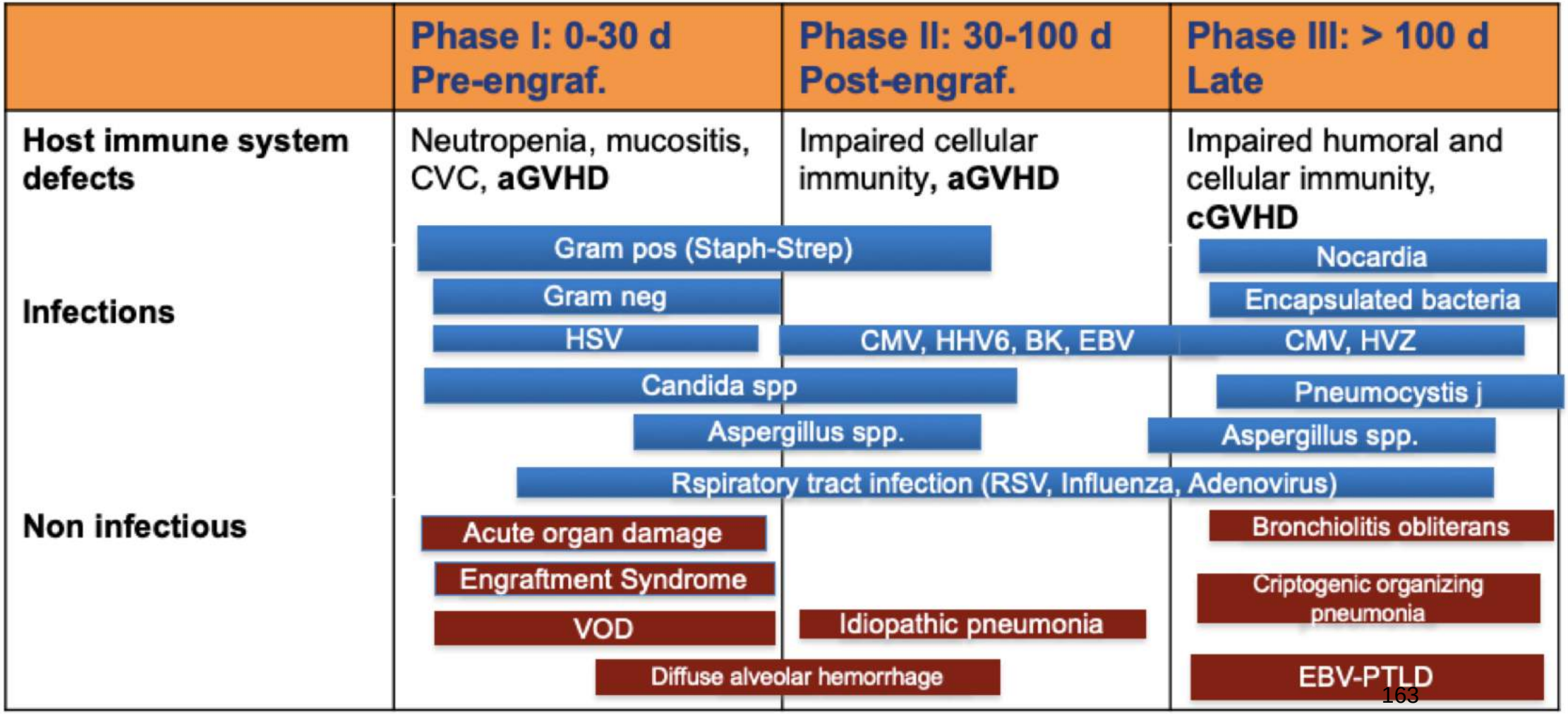
Early and acute complications

They arise during the course of treatment and resolve within a few months following the transplant treatment.

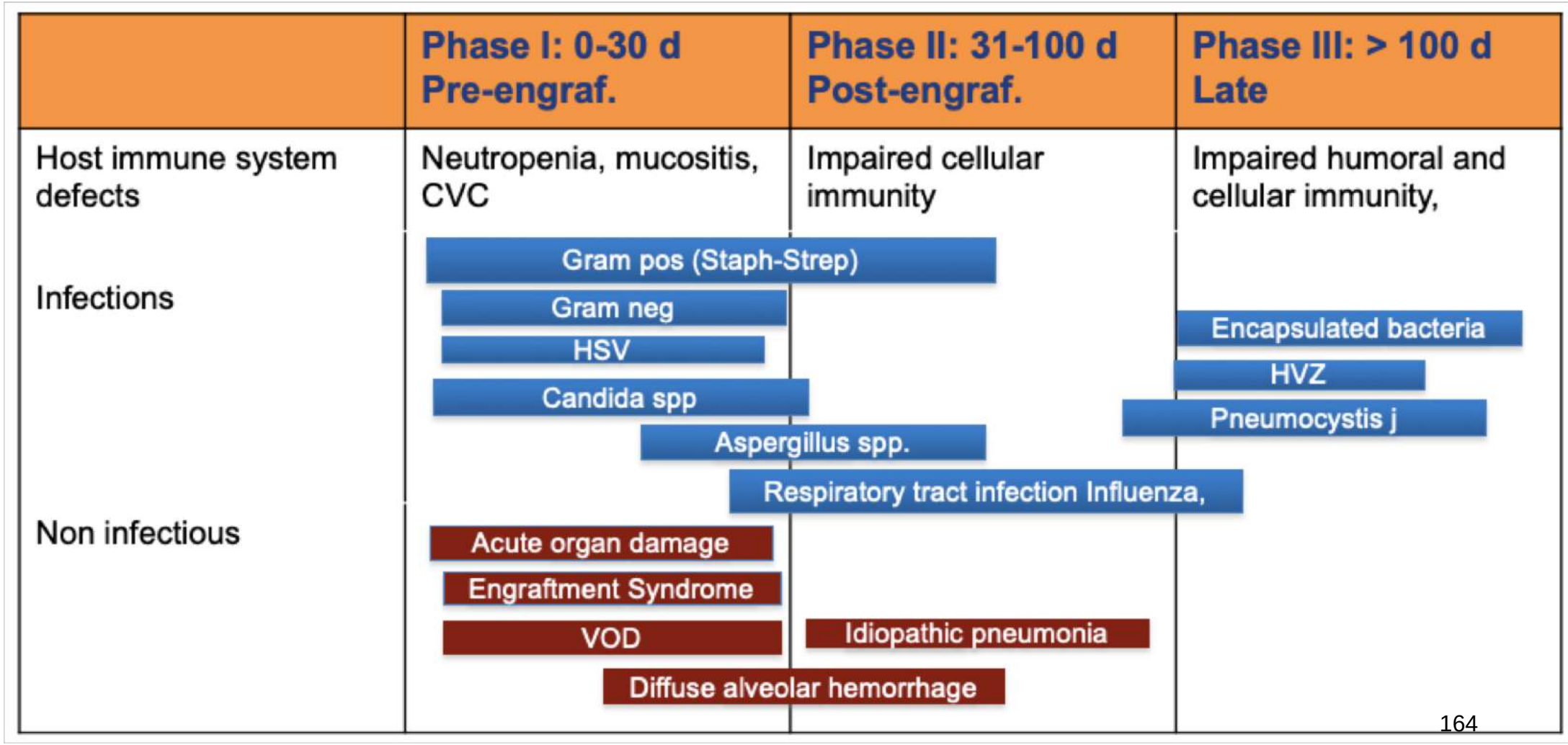
- Vomit
- Nausea
- Mucositis
- Constipation
- Diarrhea
- Myelosuppression (Neutropenia, Piastrinopenia, Anemia)
- VOD
- Infections
- Fatigue

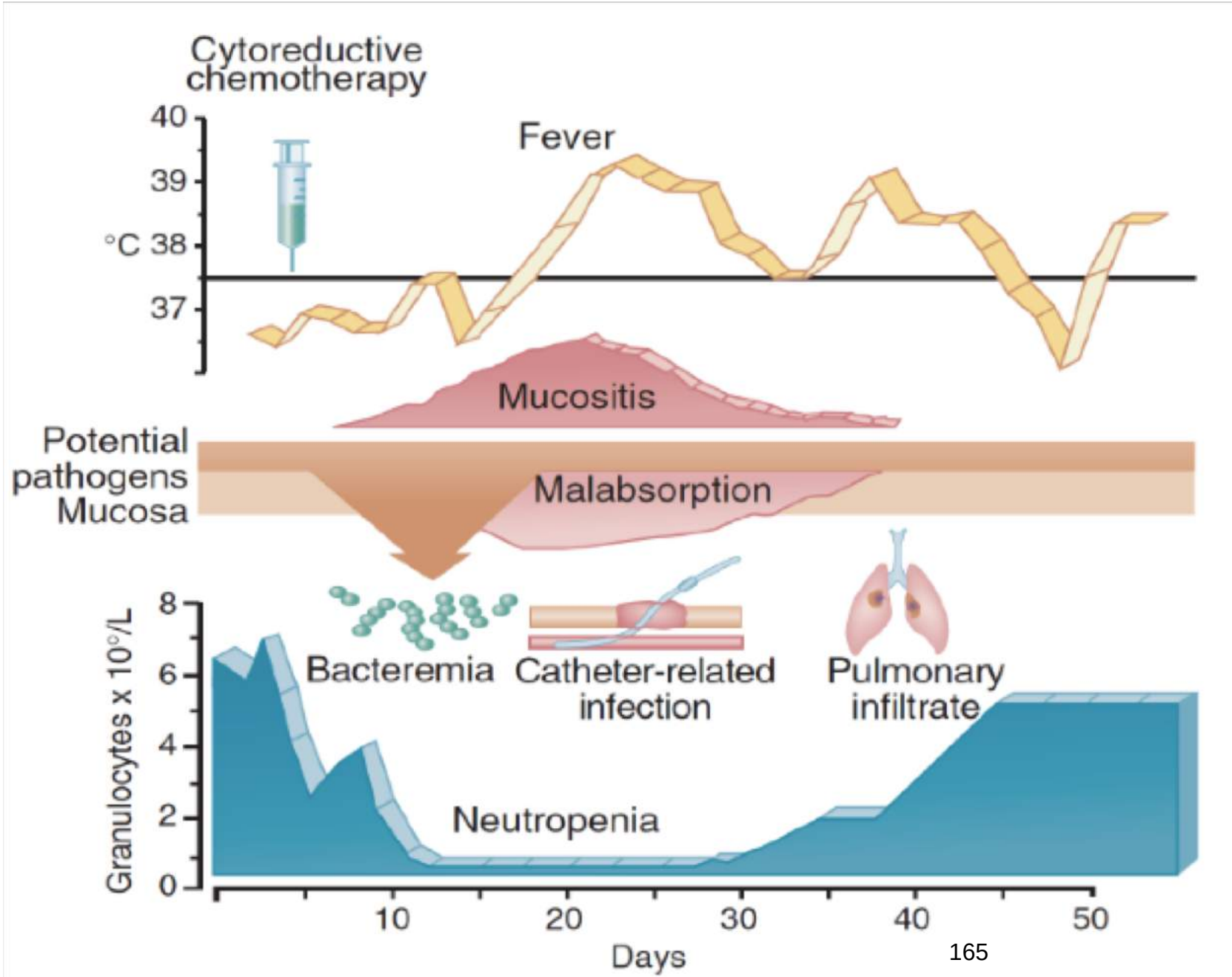
Partridge, A., Burstein, H., Winer, E., 2001 *Side Effects of Chemotherapy and Combined ChemohormonalTherapy in Women With Early-Stage Breast Cancer.* J NatlCancer InstMonogr, 30:135–42

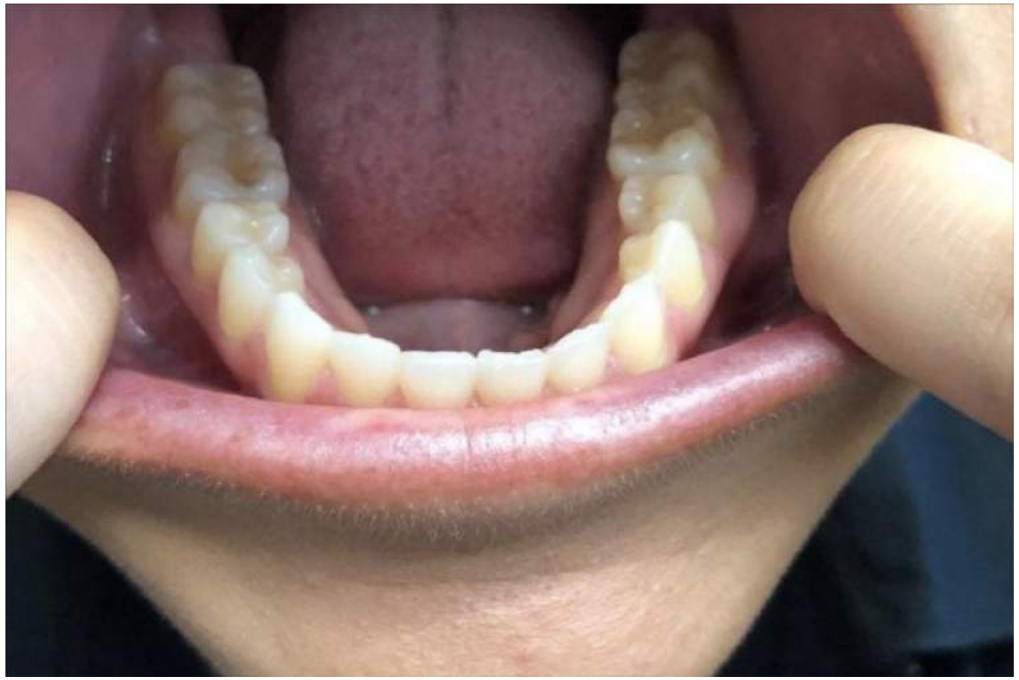
Complications – density in Allo-HSCT



Complications – density in Auto-HSCT




Cytoreductive chemotherapy
40
39
°C 38
37
Fever
Mucositis
Potential pathogens
Mucosa
Malabsorption
Bacteremia
Catheter-related infection
Pulmonary infiltrate
Granulocytes x 10°/L
8
6
4
2
0
Neutropenia
10
20
30
40
50
Days



Mucositis & Oral care

Early and acute complications in BMT setting, diagnosis and management:

- **Management of mucositis & oral care, nausea, vomiting and pain management**
- **Central venous access devices (care of CVAD: Hickman, port and PICC)**
- **Neutropenic fever, management of thrombocytopenia and bleeding**

Background & Introduction

Mucositis

Generic term for inflammation and ulceration which can affect the mucous membrane anywhere along the GI tract and affects patients undergoing to radiotherpy and/or chemiotherapy.

ORAL MUCOSITIS - OM

Is the inflammation of the mucosal membranes from the inner surface of the mouth.

STOMATITIS

In addition to the OM also include all non-by chemo or radiotherapy induced inflammatory reactions of the oral mucous membrane, the gingiva and the theeth elements.

GASTROINTESTINAL MUCOSITIS

Specific term for GI mucosal lesions caused by cytotoxic anticancer therapies.

Oral Mucositis

OM is characterised by ulceration, which may result in pain, dysfagia and impairment of the ability to talk.

Mucosal injury provides an opportunity infection to flourish, placing the patients at risk of sepsis and septicemia.

Rubenstein et al. (2004), Al-Dasoogi et al.(2013)

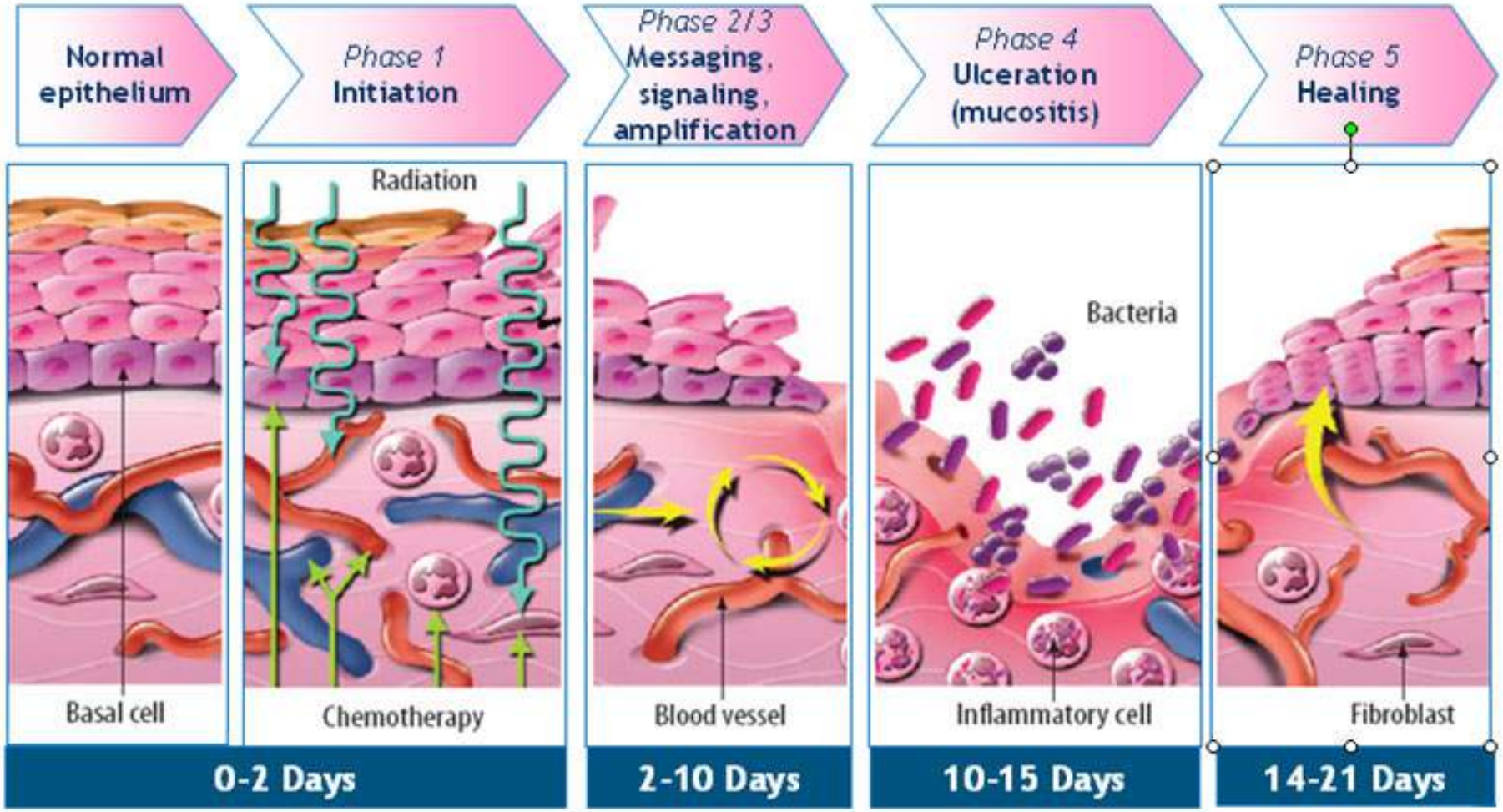
Oral complication of HSCT include

Oral Mucositis	Xerostomia
Malnutrition	Oral Graft versus Host Disease
Ulceration	Trismus
Taste changes	Halitosis
Bleeding	Dry lips/mouth
Pain	Inability to sleep
Personal impact	Length of stay
Osteonecrosis	Fibrosis
Inability to eat	Inability to speak
Infection (local & systemic)	Halitosis
Dental caries/decay	Osteonecrosis

(EOCC 2017)

ATTENTION **Mucositis usually occurs 4-10 days after the conditioning.** ATTENTION

Pathophysiology



Sonis et al. 2004

Prevalence

15 – 40 % patients' standard **chemioteraphy** treated.

70 – 90 % patients' undergoing to **HSCT** (MAC).

80 - 100 % patients' **radiotherapy** treated for neck-head cancer.

Risk for severe Oral Mucositis

30-40% chemo-/radiotherapy

50-60% head/neck radiotherapy

50-60% high doses chemotherapy

90-100% (myeloablative) allogeneic HSCT

90-100% head/neck radio-/chemotherapy

Quinn et al. 2008

How long…

Severe MO: more than 10 days.

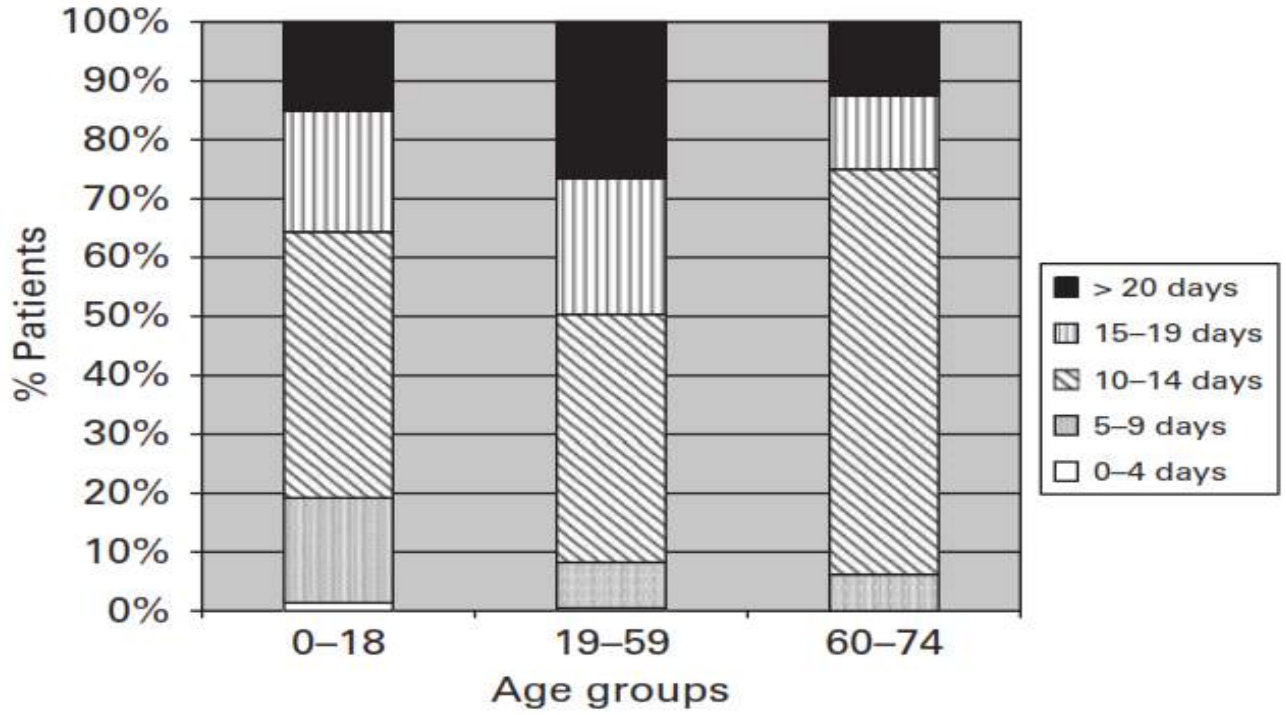
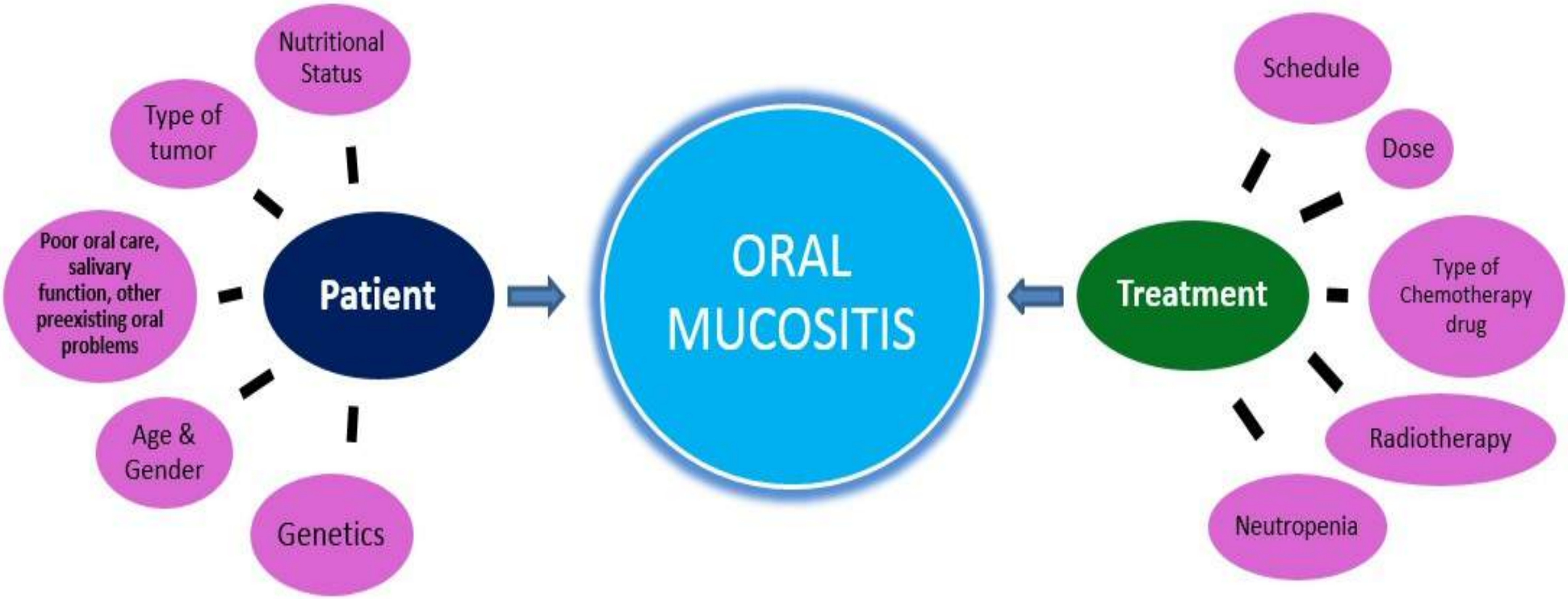


Figure 2 Duration of severe mucositis (Grades 3 and 4 according to the WHO scale).

Vagliano et al. , Incidence and severity of oral mucositis in patients undergoing haematopoietic SCT—results of a multicentre study 2011

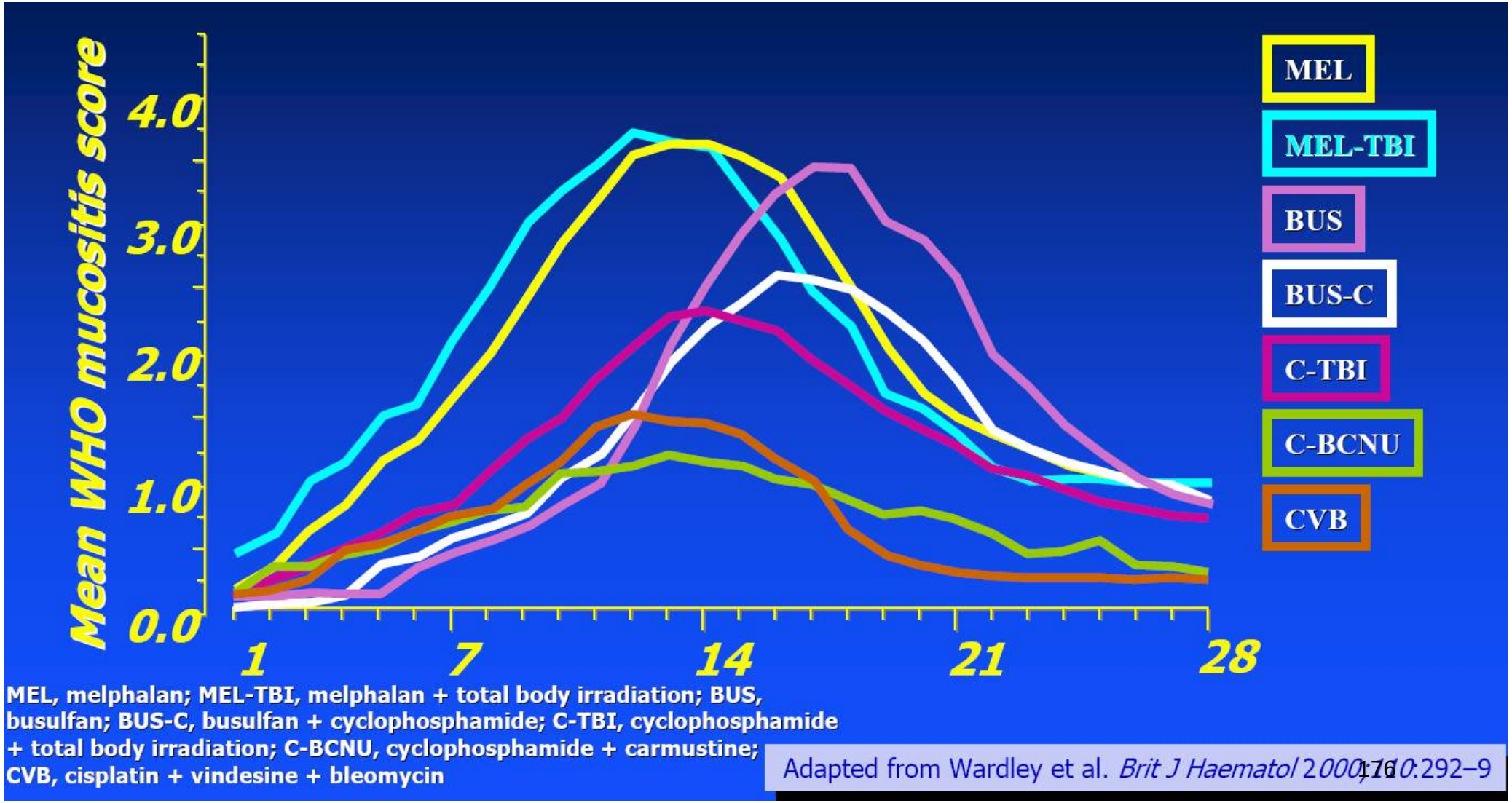
Risk Factors



Risk Factors

Principal Chemioterapy	Others Chemioterapy	Antibodies
5-Fluorouracil	Carboplatin	Alemtuzumab
Cytarabine	Idarubicin	Gemtuzumab
Doxorubicin	Paclitacsel	Trastuzumab
Radiations	Anthracycline	Trastuzumab emstansine
Ethoposide	Darcabazin	Pertuzumab
Methotrexate	Bleomicin	
Cyclophosphamide	Anthracycline	
Melphalan	Docetaxel	
Cisplatin	Capecitabine	
Irinotecan	Daunorubicin	
Busulfan	Epirubicin	
	Lomustine	
	Mitomycin	
	Mitoxantrone	
	Oxaliplatin	
	Thiotepa	
	Vincristine	

Oral Mucositis after different conditionings' regimes



Evidenced based practice & Indications

Nurses assessment

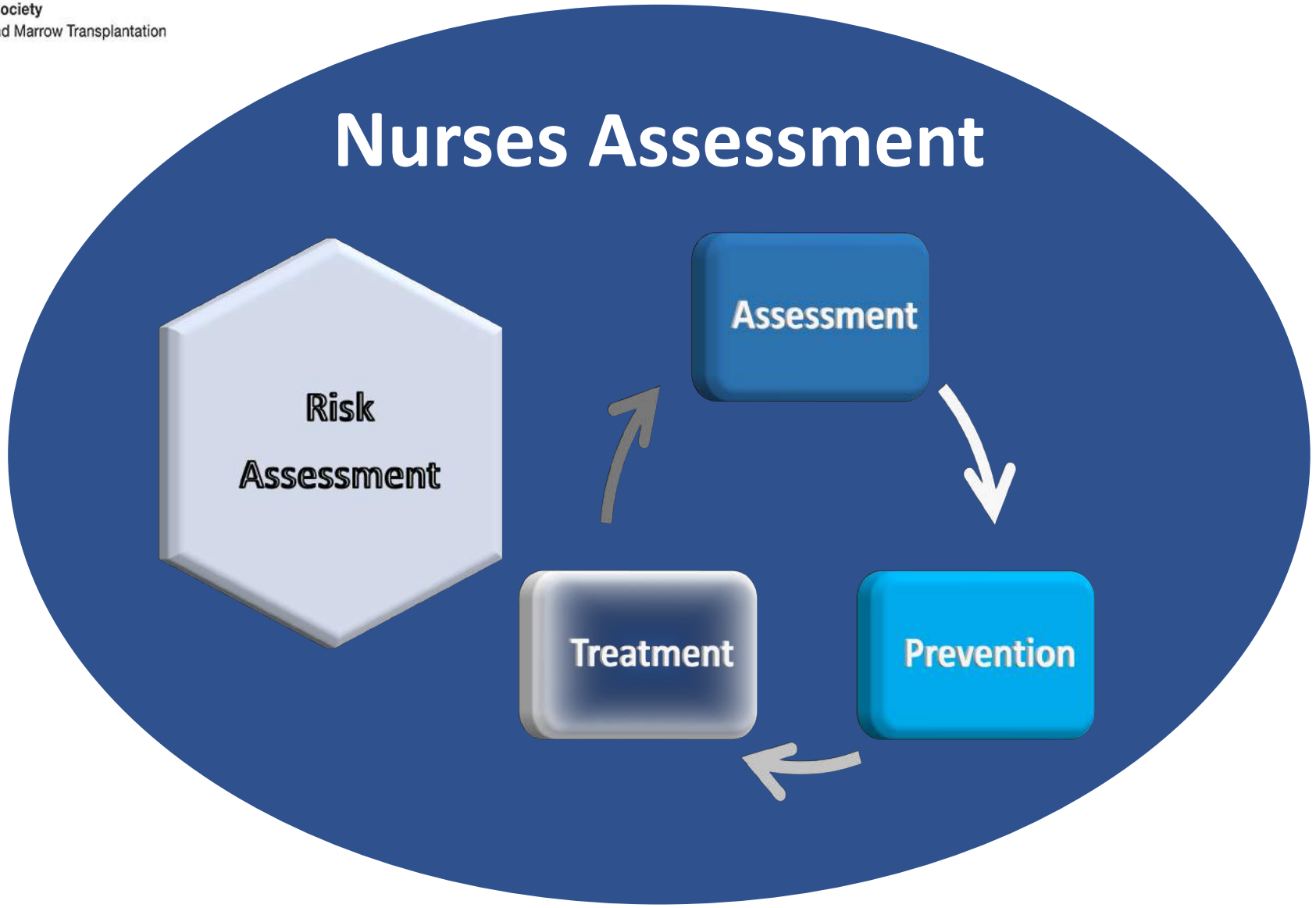
Roles of nurses in prevention and treatment mucositis:

- Education of patient's self-care.
- Identifications of High Risk patients.
- Evaluations and monitoring of mucositis.
- Management of symptoms and complications.

4 key principles

1. Accurate assessment of the oral cavity.
2. Individualised plan of care.
3. Initiating timely.
4. Preventative measures and correct treatment.

(Quinn et al. 2008)


Nurses Assessment
Risk Assessment
Assessment
Prevention
Treatment

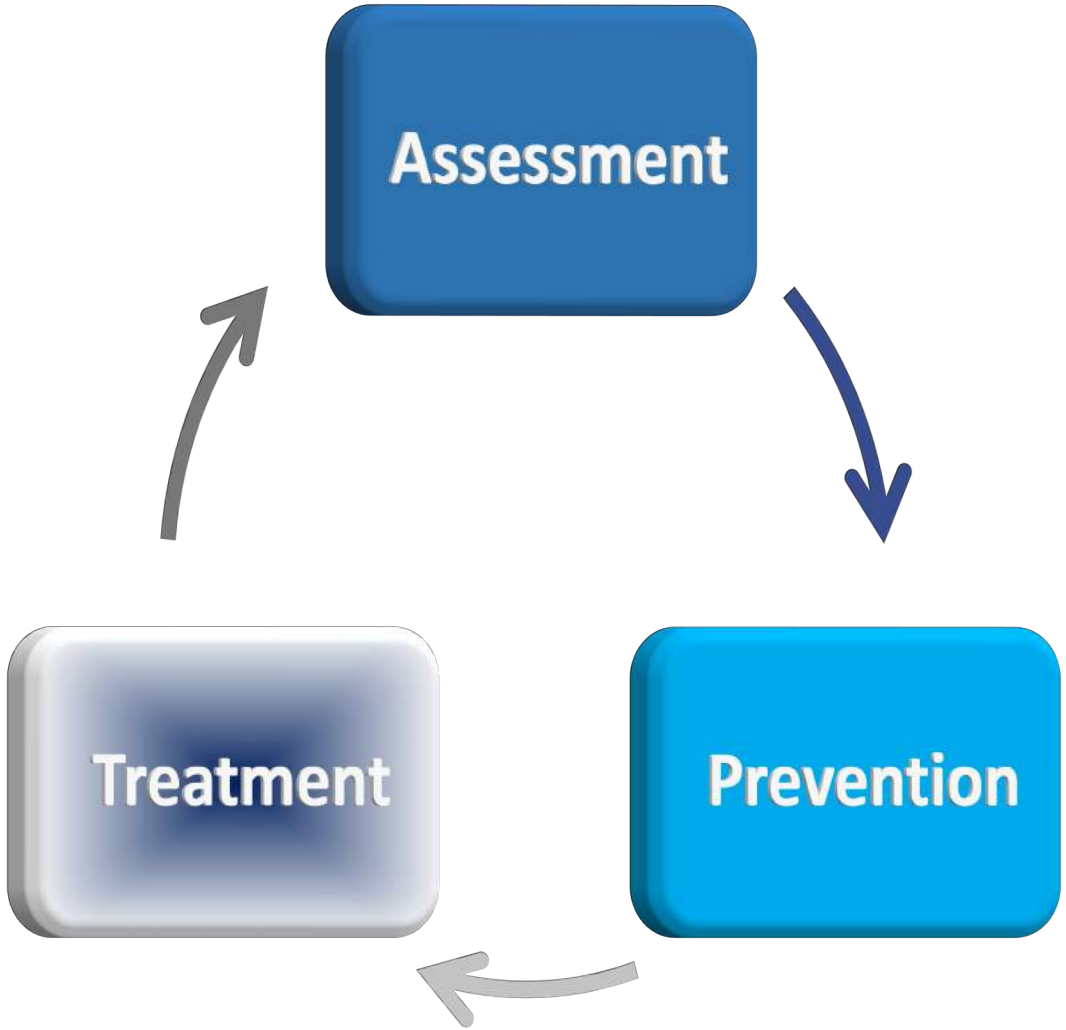
Risk Assesment

Anagrafic evaluation (direct risk): age, gender.

Anamnestic evaluation (direct risk): the initial conditions of oral cavity (presence of lesions, caries, prosthetics, hygiene habits, previous episodes of mucositis, the previous level of patient compliance and care givers.

Clinical Evaluation (indirect risk): conditioning (intensity, duration, drugs, TBI, etc ....), type of illness, comorbidities (metabolic diseases, renal failure, nutritional status, etc ... ..), previous chemotherapy, supportive drugs.

Baseline evaluation with specific tools: WHO, NCI-CTCAE, Chimes (pediatric), subjective instruments (OMDQ), management tools, NRS or VAS (pain), numerical scales for swallowing and phonation.


Assessment
Prevention
Treatment

Assessment

1. Evaluation
2. Scoring and Scales
3. Mouth Inspection
4. Alimentation ability
5. Pain

Evaluation (Assesment)

Sign & Symptoms

Pain	Nutritional probelms	Saliva	Bleeding
Could be important	Swallow problems	Quantitative deficit: dryness, xerostomia	Spontaneous or provoked
Deep	Difficulty in chewing	Qualitative deficit:loss of moisturizing, humectact and protective power(thick liquid and sticky; difficult to expel and swallowing)	Mucosa or Gums
Burning	Edema		Precence of ulcerations
Burning			Disepithelization
Full			Dripping
Often required opiates			Favored by Piastrinopenia
Dysgeusia	Dysphonia		Dysarthria
Taste perception changes	Voice changes		Difficulty in articulationg the word
“Ferrous” flavor	Difficult to make sounds		

Scoring (Assesment)

The main purpose of the scoring at the beginning of the treatment is recording of the initial situation.

The scoring before and during the treatment, gives the nurse the possibility to provide advice to the individual situation and needs of the patient.

Use the same measuring instrument.

What is the best instrument depends on the circumstances (type of patient, for research or patient care).

Score, if possible on a **daily basis** with the help of a measuring instrument, including a pain VAS

Scales (Assesment)

- Oral Mucositis Assessment Scale - **OMAS**
- World Health Organization Grading of Mucositis - **WHO**
- NCI Common Toxicity Criteria for Adverse Events - **NCI-CTCAE**
- Daily Mucositis Score – **DMS**

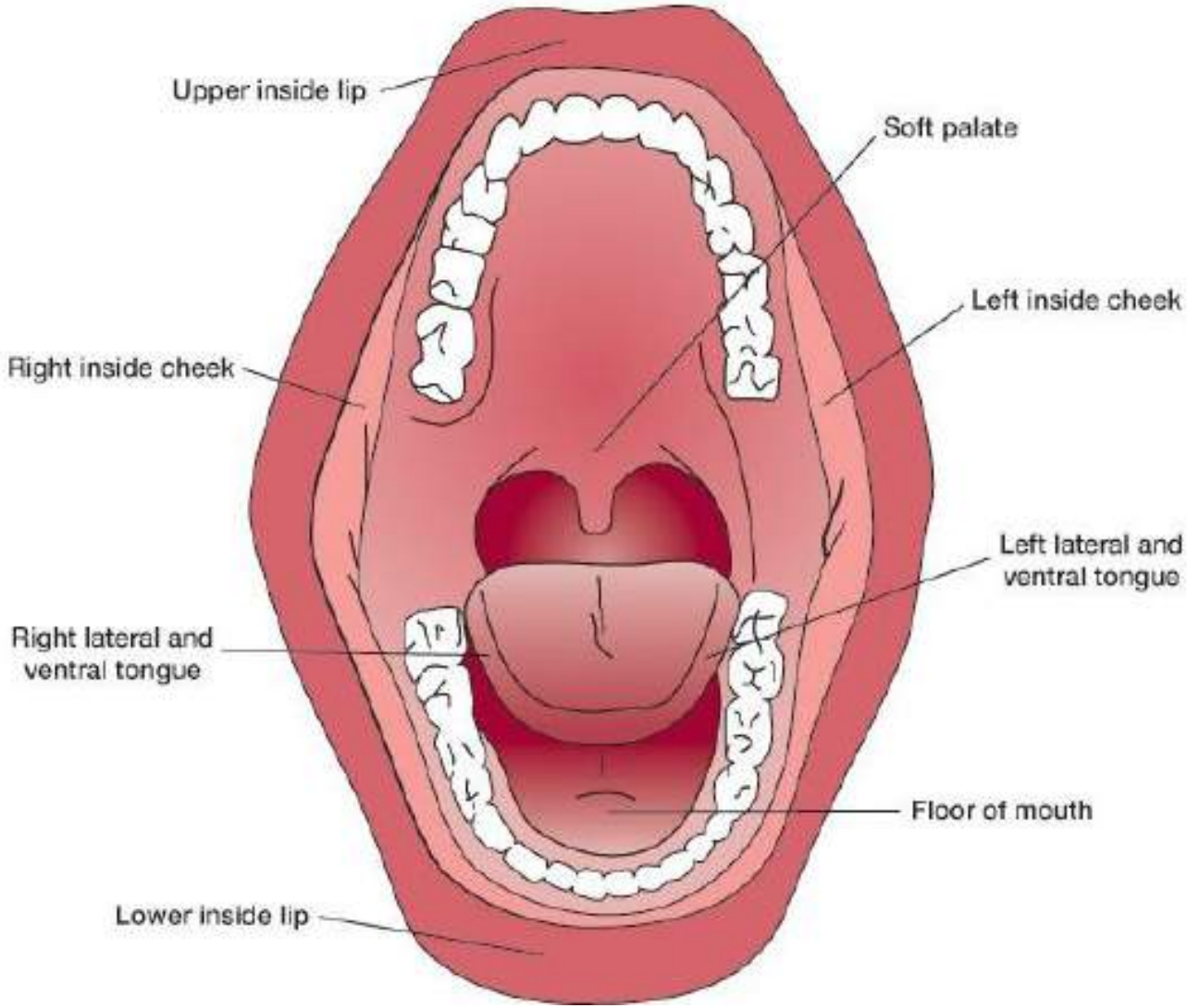
Scales (Assesment)

WHO Scale

Grade 0	no changes
Grade 1	soreness/erythema
Grade 2	soreness/erythema + ulceration + can eat solid foods
Grade 3	soreness/erythema + ulceration + can use a liquid diet only
Grade 4	soreness/erythema + ulceration + oral alimentation is not possible

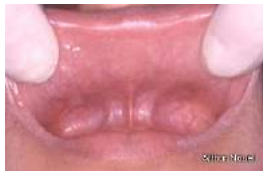
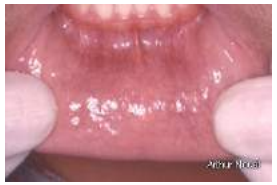
ATTENTION **WHO is the current tool to assess mucositis severity worldwide.** ATTENTION

Moth inspection

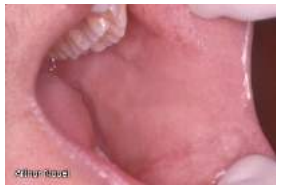


Mouth Inspection (Assesment)

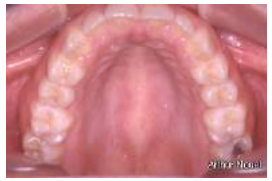
Nine anatomical areas of the mouth in scoring mucositis.

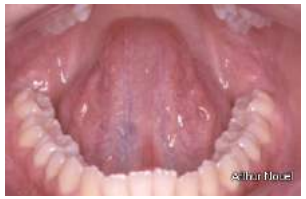
Inner lips

Inside Cheek




Palate



Bottom tongue and mouth bed


Sides and front of the tongue

Lalla et al.

Mouth Inspection (Assesment)

Performing the Physical Examination

Equipment:

- Oral mucositis assessment sheet
- Gloves
- Mask
- Light
- Tongue depressor
- 2x2 gauze

Good lighting is extremely important to see difficult sites.

Proper positioning of the patient and the operator.

Remove dentures.

Collect subjective(ask the patient information about the lesions of the oral mucosa, mouth, pain, voice, swallow, alimentation and taste) and objective data(observe humidity, color, cleaning, lesions, characteristic of saliva).

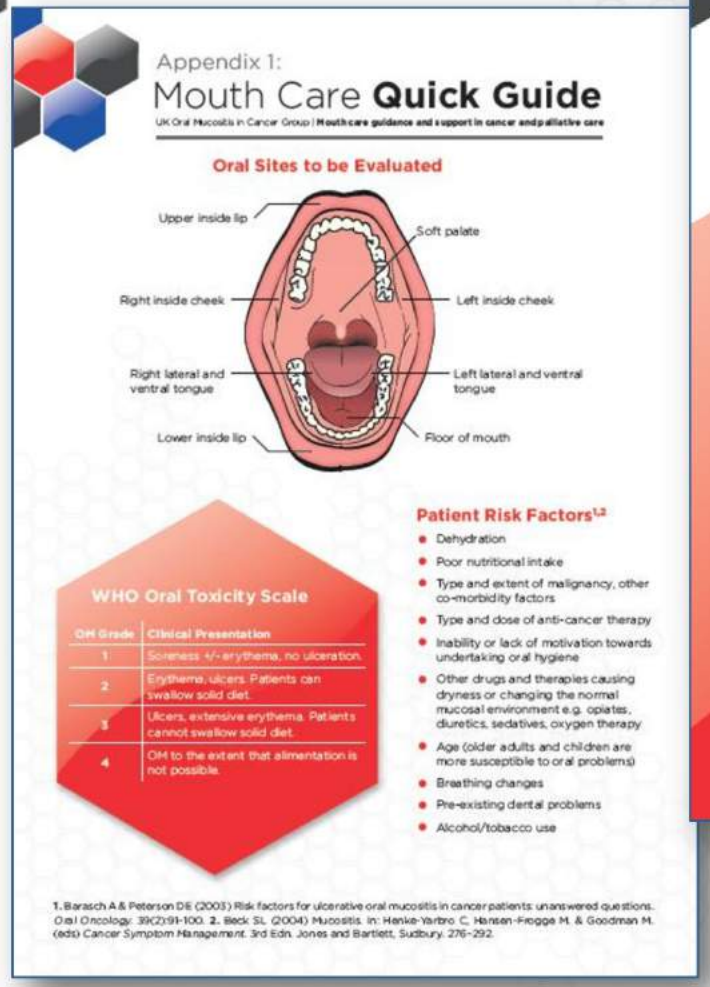
Return the documentation data.

Lalla et al.

Nurses Frontiers
www.edu-nursesnofrontiers.com
moodle

EBMT
European Society
for Blood and Marrow Transplantation

Reference guides



Appendix 1:
Mouth Care **Quick Guide**
UK Oral Mucositis in Cancer Group | **Mouthcare guidance and support in cancer and palliative care**

Oral Sites to be Evaluated

Upper inside lip
Soft palate
Right inside cheek
Left inside cheek
Right lateral and ventral tongue
Left lateral and ventral tongue
Lower inside lip
Floor of mouth

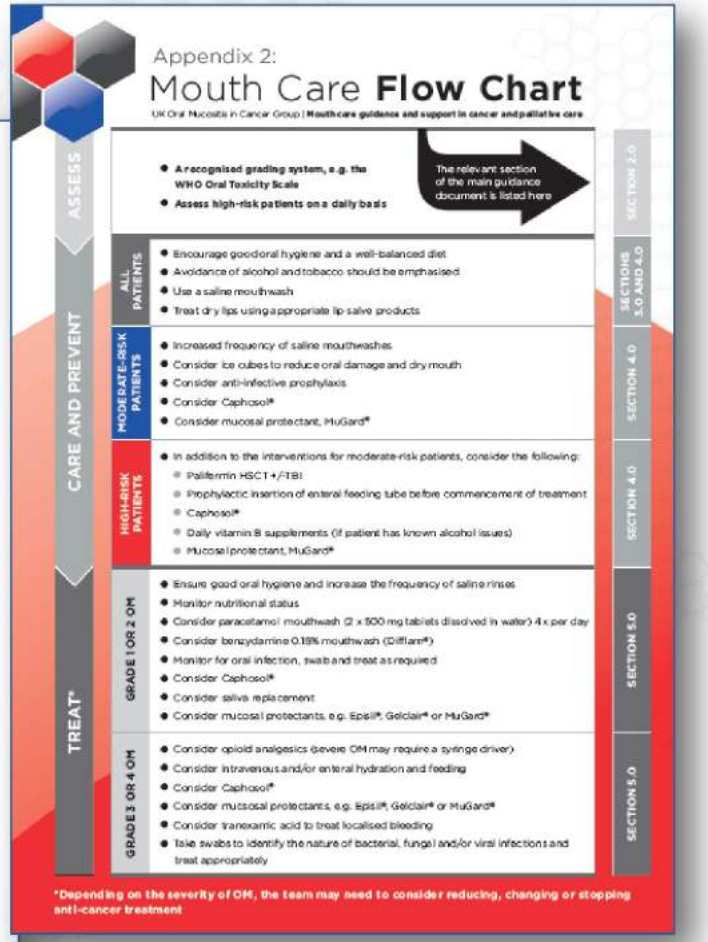
WHO Oral Toxicity Scale

OM Grade	Clinical Presentation
1	Soreness +/- erythema, no ulceration.
2	Erythema, ulcers. Patients can swallow solid diet.
3	Ulcers, extensive erythema. Patients cannot swallow solid diet.
4	OM to the extent that alimentation is not possible.

Patient Risk Factors[1,2]

- Dehydration
- Poor nutritional intake
- Type and extent of malignancy, other co-morbidity factors
- Type and dose of anti-cancer therapy
- Inability or lack of motivation towards undertaking oral hygiene
- Other drugs and therapies causing dryness or changing the normal mucosal environment e.g. opiates, diuretics, sedatives, oxygen therapy
- Age (older adults and children are more susceptible to oral problems)
- Breathing changes
- Pre-existing dental problems
- Alcohol/tobacco use

1. Barasch A & Peterson DE (2003) Risk factors for ulcerative oral mucositis in cancer patients: unanswered questions. *Oral Oncology*. 39(2):91-100. 2. Beck SL (2004) Mucositis. In: Henke-Yarbro C, Hansen-Frogge M. & Goodman M. (eds) *Cancer Symptom Management*. 3rd Edn. Jones and Bartlett, Sudbury. 276-292.



Appendix 2:
Mouth Care **Flow Chart**
UK Oral Mucositis in Cancer Group | **Mouthcare guidance and support in cancer and palliative care**

ASSESS
- A recognised grading system, e.g. the WHO Oral Toxicity Scale
- Assess high-risk patients on a daily basis

The relevant section of the main guidance document is listed here

CARE AND PREVENT

ALL PATIENTS — SECTIONS 3.0 AND 4.0
- Encourage good oral hygiene and a well-balanced diet
- Avoidance of alcohol and tobacco should be emphasised
- Use a saline mouthwash
- Treat dry lips using appropriate lip salve products

MODERATE-RISK PATIENTS — SECTION 4.0
- Increased frequency of saline mouthwashes
- Consider ice cubes to reduce oral damage and dry mouth
- Consider anti-infective prophylaxis
- Consider Caphosol®
- Consider mucosal protectant, MuGard®

HIGH-RISK PATIENTS — SECTION 4.0
- In addition to the interventions for moderate-risk patients, consider the following:
  - Palifermin HSCT+/-TBI
  - Prophylactic insertion of enteral feeding tube before commencement of treatment
  - Caphosol®
  - Daily vitamin B supplements (if patient has known alcohol issues)
  - Mucosal protectant, MuGard®

TREAT*

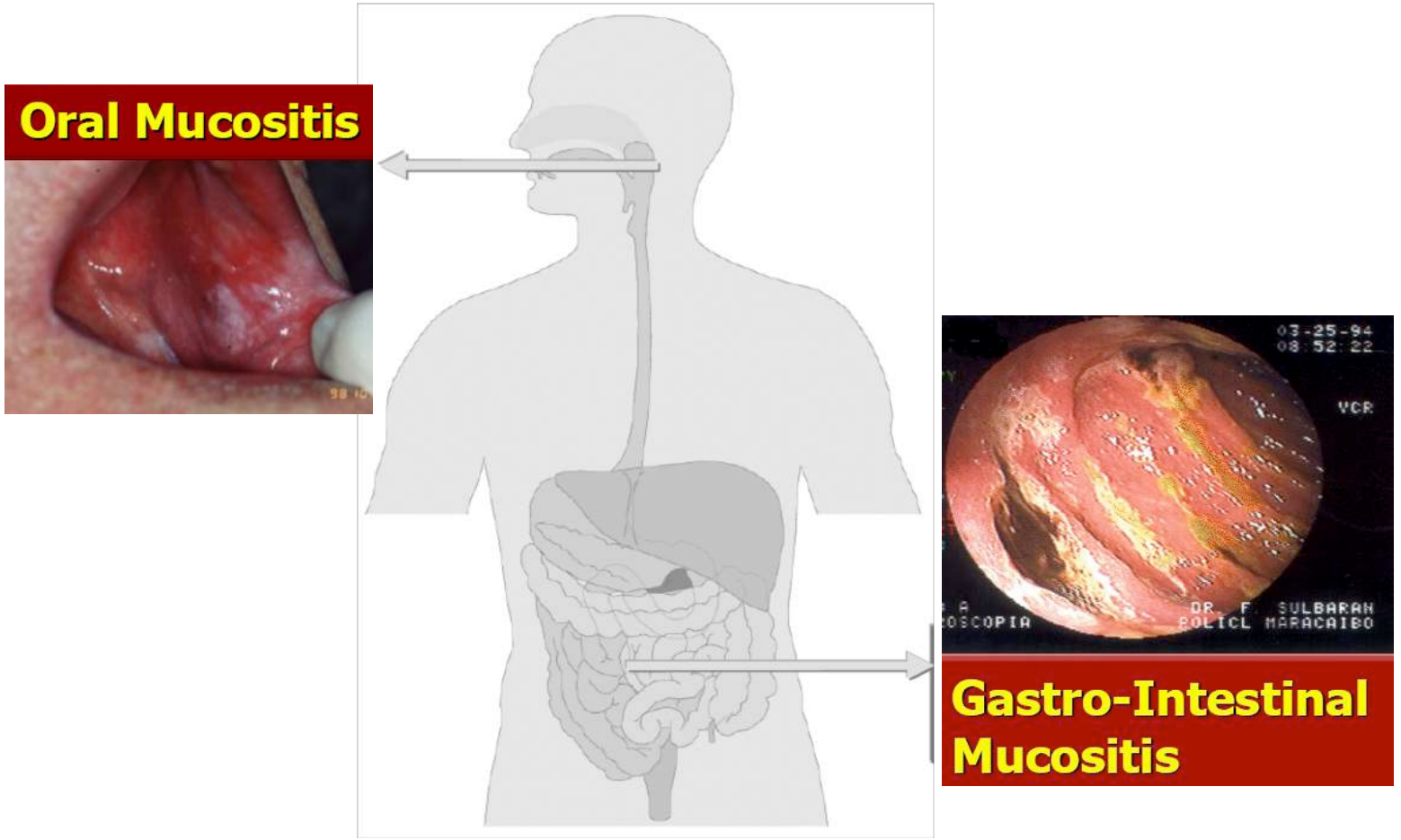
GRADE 1 OR 2 OM — SECTION 5.0
- Ensure good oral hygiene and increase the frequency of saline rinses
- Monitor nutritional status
- Consider paracetamol mouthwash (2 x 500 mg tablets dissolved in water) 4 x per day
- Consider benzydamine 0.15% mouthwash (Difflam®)
- Monitor for oral infection, swab and treat as required
- Consider Caphosol®
- Consider saliva replacement
- Consider mucosal protectants, e.g. Episil®, Gelclair® or MuGard®

GRADE 3 OR 4 OM — SECTION 5.0
- Consider opioid analgesics (severe OM may require a syringe driver)
- Consider intravenous and/or enteral hydration and feeding
- Consider Caphosol®
- Consider mucosal protectants, e.g. Episil®, Gelclair® or MuGard®
- Consider tranexamic acid to treat localised bleeding
- Take swabs to identify the nature of bacterial, fungal and/or viral infections and treat appropriately

*Depending on the severity of OM, the team may need to consider reducing, changing or stopping anti-cancer treatment

UK Oral Mucositis in Cancer Group
UKOMiC
Oral Mucositis is no laughing matter...

Gastrointestinal mucositis grading (Assesment)



Gastrointestinal mucositis grading (Assesment)

oral and gastrointestinal mucositis in patients undergoing haematopoietic stem cell transplantation

Incidence of WHO grade 3 or 4 oral mucositis can be as high as 75% in patients undergoing haematopoietic stem cell transplantation (HSCT), depending on the intensity of the conditioning regimen used and the use of methotrexate prophylactically to prevent graft-versus-host disease. Management of oral and gastrointestinal mucositis is one of the main challenges during the period of aplasia, with risk of sepsis related to degree of mucosal barrier breakdown and depth of marrow suppression.

gastrointestinal mucositis grading

In contrast, there is a limited number of instruments available for assessment of gastrointestinal mucositis. These scales typically measure indirect outcomes of mucosal injury, including diarrhoea. However, interpretation of such data can be confounded by other clinical conditions and interventions that also contribute to the event being measured. New technologies may lead to enhanced assessment strategies for gastrointestinal mucositis. Tracheal mucositis, pharyngeal mucositis, laryngeal mucositis, small intestinal mucositis, rectal mucositis, and anal mucositis are terms that can be scored separately in the CTCAEv4.03 within the system organ class 'Gastrointestinal disorders–Other, specify'. Diarrhoea is a term that is scored frequently within gastrointestinal mucositis also, which should not be confused with loose stool. The Bristol stool chart [29] is

Alimentation Ability (Assesment)

Maintain an **adequate supply of nutrients** throughout the patient recovery.

Development of a **nutritional care plan**.

Monitor the nutritional status

Encourage the patients to maintain a **balanced diet**.

Prevention and treating **emesis**.

Nutrition assessment:

- Nutritional intake and weight be monitored
- Avoid hard, sharp, spicy or hot food and alcool and tobacco
- Taste changes
- Soft diet, liquid supplements

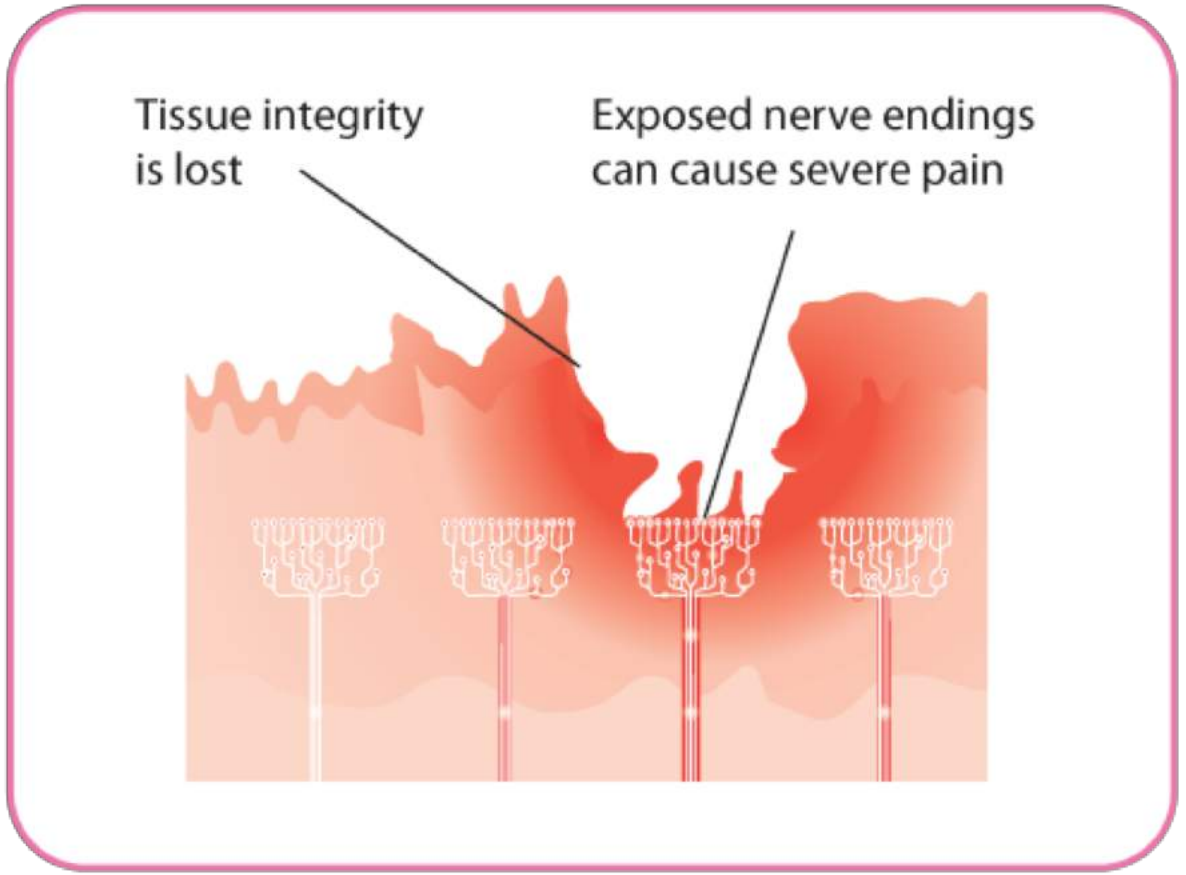
Pain (Assesment)

Daily monitoring of pain.
Grading with NRS scale.

The panel **recommends** that patient-controlled analgesia with **morphine** should be used to treat pain due to oral mucositis in patients undergoing HSCT (II).

The panel **suggests** that transdermal fentanyl may be effective to treat pain due to oral mucositis in patients receiving conventional or high-dose chemotherapy, with or without total body irradiation (III).

The panel **suggests** that 0.5% doxepin mouthwash may be effective to treat pain due to oral mucositis (IV).



Prevention

UKOMiC

Oral care

Low Level Laser Therapy

Prevention

- Patient education
- Nutritional Screening and food choose
- Oral care
- Interdental care
- Denture
- Mouthwashes
- Early identification and treatment of dry mouth or lips
- Adequate nutritional intake
- Oral hygiene protocol

UKOMiC (Prevention)

Risk Classification	Risk Factors
Low risk of Oral damage and/or OM e.g. WHO grade 1	Patients with no prior OM. Patients who are receiving treatments not know to cause moderate or severe OM.
Moderate risk of Oral damage and/or OM e.g. WHO grade 2	Patients with a previous history of grade 2 OM. Patients receiving agents know to cause OM such as Capecitabine, 5-Fluorouracil, Docetaxel, Cyclophosphamide, anthracycline containing regimens, and targeted treatments including Epidermal Growth Factor Receptor (EGFR) inhibitors. Palliative radiotherapy to the head and neck region. Pharmacological agents and/ or co-morbidities predisposing the patient to xerostomia. The very young and the elderly.
Severe risk of Oral damage and/or OM **e.g. WHO grade 3-4**	Patients with previously documented grade 3 or 4 OM and/or patients with resistant grade 2 OM. Patients who are undergoing survey to the oral cavity or head and neck region. Patients receiving high dose chemotherapy agents prior to autologous HSCT, reduced and full intensity, allogeneic HSCT (with/without Total Body Irradiation) High dose methotrexate and cytarabine containing regimens. Radical Radiotherapy to the head and neck region with/without chemotherapy.

UKOMiC (Prevention)

Risk Classification: **Low risk** of Oral demage and/or OM e.g. WHO grade 1

Intervention
Good oral hygiene All patients should be educated and encouraged to maintain good oral hygiene. (Oral Care)
Smoking cessation
Plaque reduction Taste changes experienced by many patients may result in a higher intake of sugar foods and the build-up of dental plaque. A soft or medium toothbrush with fluoride containing toothpaste is recommended
High-fluoride toothpaste, foam, gel
Salt water mouthwash One teaspoon salt to added 900ml of cold or warm water. Salt water mouthwashes used at least 4 times in 24 hours to clean the mouth and remove debris. A fresh supply to be made daily. Each salt water rinse (patients in hospital may use 0,9% sodium chloride from vial) to be followed by rinsing with could or warm water.
Nutritional assessment and referral to a dietician when appropriate

UKOMiC (Prevention)

Risk Classification: **Moderate risk** of Oral demage and/or OM e.g. WHO grade 2

Intervention
Increasing the frequency of saline mouthwashes
Ice chips Are recommended for 5 -fluorouracil bolus treatment and for high dose Melphalan. Swish ice chips in the mouth for 30 minutes, beginning 5 minutes before treatment is administered.
Benzydamine 0.15% oral solution (Difflam®) Use 10 ml rinsed around the mouth and spat out 4 times a day. In the head and neck setting, Difflam is recommended for patients receiving radiation only (up to 50Gy).
Caphosol® (4–10 times a day) Recommended to start on the first day of chemotherapy or the first day of radiotherapy to head and neck region.
Consider mucosal protectants Including Gelclair®, Oralife gel® MuGard® (available in USA).

UKOMiC (Prevention)

Risk Classification: **Severe risk** of Oral demage and/or OM

Intervention
Nutritional assessment. Referral to a dietician where appropriate. All patients should be nutritionally screened using a validated screening tool e.g. Malnutrition Universal Screening Tool (MUST) and those identified as being at risk should receive early intervention for nutritional support from an experienced dietician. All HSCT patients and all head and neck cancer patients should be reviewed by a dietician prior to commencing treatment, seen at regular intervals during treatment, and may require on-going support after treatment is completed.
Anti-infective prophylaxis According to local policies/ guidance.
Palifermin HSCT +/- TBI 60 µg/kg/day Recommended for 3 days before conditioning treatment and for 3 days after transplant.
Daily Vitamin B supplements For patients with alcohol misuse issues.


ORAL CARE

Oral Care (Prevention)

General measures

- Auto-daily oral inspection.
- Elimination of sources of infection or trauma (broken teeth, broken prosthesis).
- Tartar removal at least 15 days prior to admission.
- Soften lips with lip balm or Vaseline balm.
- Often Sip water to keep the mucosa moisturized
- If patients are not self-sufficient in oral hygiene it is necessary that a nurse or a properly trained CG help them.

Care of the Oral Cavity

For All

- 0.9% sodium chloride or salt water rinses are recommended.
- Patients who find it difficult to carry out their mouth hygiene may find oral sponges easier to use than toothbrushes. These should be checked to ensure they are secure, to avoid choking and aspiration. An oral sponge should only be used once and not left in the cleaning solution. It should be noted that oral sponges are not equivalent to tooth-brushing and are not therefore effective for plaque control or the prevention of caries.
- Where patients can not undertake their own oral hygiene, a nurse or carer can assist. The mouth may be irrigated with saline with or without suction.
- Adequate oral fluid intake and a well balanced diet should be encouraged.
- Alcohol should be minimized and tobacco should be avoided. **Spicy foods may irritate the mouth and care should be taken with rough or crunchy foods as they may damage the mucosal lining or gum**.
- All patients should be nutritionally screened using a validated screening tool e.g. Malnutrition universal screening tool (MUST) and those identified as being at risk should receive early intervention for nutritional support from an experienced dietitian.
- For any concerns regarding dysphagia, patients should be referred to the Speech and Language Therapist.

Oral Care (Prevention)

Oral hygiene

- Brush your teeth, gums and tongue after every meal and at bedtime with a soft-bristled brush to prevent injuries and bleeding (in thrombocytopenia use sponge pads)
- Use a fluoride toothpaste neutral and non-foaming, avoid toothpastes abrasive paste (granules). If the taste is not permissible to use a pediatric toothpaste.
- Brushing the teeth according to the Bass method. If you use an electric toothbrush to follow the manufacturer's directions
- Rinse the brush properly after use and store it upside on. Do not store toothbrushes in disinfecting solutions. The toothbrush should be replaced once a week during the HSCT.
- The use of dental floss is conditioned to the ability of the patient. Dental floss is not recommended if the patient is not capable and in pancytopenia.

1) Place the toothbrush against your gumline at a 45-degree angle. Move the brush back and forth gently in short (tooth-wide) strokes.

2) Brush the outer tooth surfaces, keeping the toothbrush at a 45-degree angle to the gums.

3) Brush the inner tooth surfaces, still with the toothbrush at a 45-degree angle.

4) Brush the chewing surfaces.

5) Use the top part of the brush to clean the inside surface of the top and bottom front teeth. Use a gentle up-and-down motion.

6) Brush your tongue to remove bacteria and freshen your breath.

Care of the Oral Cavity

Dentate Individuals (with teeth)

- Brush teeth at least twice a day and increase as necessary with a pea sized amount of fluoride toothpaste (1,350 -1,500ppm fluoride).
- Spit out after brushing, do not rinse.
- If brushing becomes difficult advise use of a very soft toothbrush (i.e. baby toothbrush or silk filament toothbrush).
- If an oral opportunistic infections develops, patients should use a fresh toothbrush and the infection treated appropriately.
- Some head and neck patients undergoing radiation may require toothpaste with a higher content of fluoride (over 1,500ppm) in order to protect the teeth.
- Correct dental flossing once a day may help with plaque reduction. In patients with thrombocytopenia or a clotting disorder flossing may be contraindicated. Flossing may also be contraindicated in patients receiving radiotherapy, therefore check with a member of the clinical team.

Edentulous Individuals (absence of teeth)

- Dentures should be rinsed after meals and cleaned thoroughly, twice a day, by brushing with unperfumed soap with small to medium headed toothbrush.
- Dentures should be removed when uncomfortable due to oral damage, removed over night and soaked in water.
- If a fungal infection is present, dentures must be cleaned thoroughly – soak in chlorhexidine mouthwash (if dentures have metal components) or sodium hypochlorite (i.e. Milton) for 15 minutes twice a day. Toothbrushes should also be replaced.

Oral Care (Prevention)

Rinses and mouthwashes

- Mouthwashes are usually not necessary
- Preferring rinse with sodium chloride solution or sodium bicarbonate
- If mouthwash used, rinse mouth with 15 ml of product for about 1 min, do gargle and spit. Avoid eating or drinking for at least 30 min after.

Dentures movable

- Use dentures only during meals
- Clean dentures after every meal with toothbrush and toothpaste, rinse and place in a closed container containing a special solution for dentures overnight

Oral Care (Prevention)

Identify and treat early dryness

- Use creams or cocoa butter for the lips.
- Encourage oral hydration sipping water often.
- Encourage frequent rinses with saline or bicarbonate.
- Use saliva substitutes or artificial lubricants in severe cases.
- Use ice lolly if does not cause discomfort.
- Chewing sugarfree gum or suck pieces of fruit e.g. pineapple or lemon.
- Removal viscous secretions with saline aerosol or rinse with bicarbonate solution.

Care of the Oral Cavity

Dry Lips

Patients undergoing treatment/s can experience dry lips. Yellow/white soft paraffin or normal lip salve can be used to moisten the lips. These products are contraindicated if the patient is receiving radiotherapy to the head and neck region. A water soluble lubricant may be considered. Patients receiving oxygen should be advised to use a water-soluble lubricant.

Dry Mouth

Oral hydration should be encouraged and early intervention to prevent the development of dry mouth is important. Salivary gland sparing radiotherapy techniques (such as intensity modulated radiotherapy (IMRT), which reduce the long term effects of dry mouth, have been established in recent years.

Teams should pay particular attention to relieving a dry mouth in patients with contributory risk factors including; opioids; antidepressants; steroid inhalers; oxygen and those who are nil by mouth and the terminally ill. The following interventions may provide some relief:

- **Sipping water or moistening the oral cavity** (in patients who are unable to swallow).
- **Saline mouthwashes and saline sprays**.
- **Saline nebulisers may help with thick or crusty secretions**.
- **Saliva replacement** – Dentate individuals should avoid preparations with an acidic pH, due to the increased risk of dental decay. A fluoride containing preparation is preferable for these individuals e.g. AS Saliva Orthana, Bioxtra mouth rinse.
- **Sucking crushed ice, frozen tonic water** - Caution: in patients who have already developed OM this may cause further discomfort and damage to teeth.
- **Artificial lubricants**.
- **Sugar free chewing gum** – this can stimulate saliva production. May be contraindicated in the head and neck cancer setting due to thickened secretions or the complete absence of saliva, which may increase the risk of choking.
- **Chewing fresh pineapple chunks** – this may help to stimulate saliva but can cause irritation in patients with ulceration of the mouth and damage teeth.
- **Addressing the underlying causes of taste changes** – patients should be educated and encouraged about simple dietary changes. Patients receiving radiotherapy to the head and neck may experience taste alterations or complete loss of taste. In this group of patients, the team should continue to encourage good hydration and nutrition either orally or via enteral feeding.
- **Ensuring thickened secretions are removed** – steam inhalation or saline nebulisers can loosen secretions and help with expectoration. Sodium bicarbonate mouthwash (1 tablespoon of sodium bicarbonate added to 900ml of cooled boiled water used every 3-4 hours may assist in clearing thickened secretions). Caution: there is some evidence to suggest that the use of sodium bicarbonate may affect the pH of the mouth and interfere with mucosal healing.

LLLT - Low Lever Laser Therapy (Prevention)

Luminous or infrared emissions which is supposed to be transposed by tissue chromophores receptors promoting biological effects.

To this day are unknown the action mechanisms.

- Increase of interest and number of studies
- Few blind RCT
- BIAS risk

Heterogeneity of approaches:

- Dose
- Time
- Wavelengths
- Device
- Training
- Diseases
- Antineoplastic treatments

Treatment of Oral Mucositis and Oral Complications

Mild/Moderate Mucositis - Oral Complications (Grade 1-2)

- Ensure oral hygiene is adequate including plaque removal.
- Consider increasing the frequency of saline rinses.
- Consider the need to remove dentures if they are irritating.
- Offer support with smoking cessation.
- Closely monitor nutritional status and refer to dietician if eating and drinking are affected.
- Provide simple analgesia, which may include soluble paracetamol 1 g four times daily (tablets should be dissolved in water and used as a mouthwash before swallowing). It should be remembered that paracetamol may mask fever. Escalate to soluble cocodamol 30/500 if required. The use of non steroidal anti-inflammatory drugs may be contraindicated due to the risk of bleeding and renal impairment
- Consider Benzydamine 0.15% oral solution (Difflam®), 10ml rinsed around the mouth and spat out. Repeat as required. If the patient complains of stinging, dilute 10 ml of Difflam® with 10 ml of water prior to administration and use 10 ml. However, this may be poorly tolerated in patients receiving head and neck radiotherapy and any patient with severe mucositis.
- Consider the use of low level laser therapy.
- Consider increasing folinic acid rescue for methotrexate-induced mucositis.
- Check to see if the patient has evidence of oral infection and if so ensure an anti-infective agent is prescribed.
- Consider Caphosol® (4–10 times a day) to prevent grade 1 and 2 OM becoming more severe.
- Consider applying a coating protectant.
- Consider a saliva replacement/substitute.

Treatment of Oral Mucositis and Oral Complications

Severe Mucositis/Oral Complications (Grade 3-4)

In addition to the recommendations for mild/moderate the following should be considered:

- Use of stronger analgesia, including Oxynorm®, Sevredol® and Oramorph® to alleviate pain (some liquid based analgesia may have an alcohol base which should be used with caution as it may cause irritation to the mucosa). If patients continue to suffer with pain from mucositis, consider using further opioid analgesia and review administration route, such as fentanyl patches, patient-controlled analgesia or a syringe driver (seek advice from the acute pain team or the palliative care service). Laxative medications should be prescribed as standard to prevent constipation and associated nausea.
- Ensure intravenous and/or enteral hydration and feeding is prescribed, as oral intake may be reduced (following consultation with the dietician).
- Consider Caphosol® (4–10 times a day).
- Consider applying a coating protectant, e.g. Gelclair®, Oralife gel®, MuGard® Episil®. The product should be rinsed around the mouth to form a protective layer over the sore areas, and generally applied 1 hour before eating. These products are not to be swallowed.

Treatment of Oral Mucositis and Oral Complications

Bleeding from the Mouth

If there is associated bleeding in the oral cavity, consider using 500mg of Tranexamic acid for injection or tablets (these can be added to 5ml water or dissolved). Use as a mouthwash every 4-6 hours to treat localized bleeding.

Anti-Infective Treatment

Despite prophylaxis, patients may still present with an infection of the mouth. The team should work closely with the microbiology team to ensure oral infections are treated appropriately. The team should be particularly vigilant for any patient who may be immunocompromised due to disease and/or treatment. Swabs should be taken from the mouth to identify bacterial, fungal and viral infections.

Treatment options include the following:

Fungal infections

Consider the use of systemic anti-fungal agents. Refer to locally agreed anti-fungal guidance.

Bacterial

Consider the use of antibiotics in line with locally agreed guidance.

Viral infections

Consider topical anti-viral agent for local infection in low-risk patients. Consider systemic anti-viral agents (for high-risk patients) in line with local policy.

GvHD

Particular attention needs to be paid to identifying oral problems relating to graft versus host disease (GvHD) in the allogeneic HSCT setting while these principles will still apply, anti GvHD treatment may be required.

Conclusion

- **Continue oral hygiene**
- **Infections management:**
  - Culture and sensitivity patterns for oral/IV therapy
- **Bleeding management:**
  - Consider tranexamic acid to treat localised bleeding
  - Platelet counts
- **Inflammation:**
  - Anti-inflammatory treatment as required
- **PAIN CONTROL**
- **Nutrition intake**
  - Parenteral nutrition
- Benefit of a quality management system: following SOPs (Standard Operative Procedures)

Literature reference

- Al-Dasoogi N, et al. Emerging evidence of the pathobiology of mucositis. Support Care Cancer. 2013;21:3233–41.
- Bhatt V, Ventrell N, et al. Implementation of a standardized protocol for prevention and management on oral mucositis in patients undergoing hematopoietic stem cell transplant. J Oncol Pharm Pract. 2010;16(3):195–204.
- Blijlevens NM, Sonis ST "Palifermin (recombinant keratinocyte growth factor -1): a pleiotropic growth factor with multiple biological activities in preventing chemotherapy and radiotherapy induced mucositis". Annals of Oncology 18: 817–826, 2007 doi:10.1093/annonc/mdl332.Published online 9 October 2006. Review
- Choi, S., & Kim, H. (2012). Sodium bicarbonate solution versus chlorhexidine mouthwash in oral care of acute leukemia patients undergoing induction chemotherapy: A randomized controlled trial. Asian Nursing Research, 6(2), 60-66.
- Farrington, M., Cullen, L., & Dawson, C. (2010). Assessment of oral mucositis in adult and pediatric oncology patients: an evidence-based study. Head and Neck Nursing, 28 (3), 8-15.
- Filicko J, Lazarus HM, Flomenberg N. Mucosal injury in patients undergoing hematopoietic progenitor cell transplantation: new approaches to prophylaxis and treatment. Bone Marrow Transplant. 2003;31:1–10.
- Gibson, F., Auld, E., Bryan, G., Coulson, S., Craig, J., & Glenny, A. (2010). A systematic review of oral assessment instruments: what can we recommend to practitioners in children's and young people's cancer care? Cancer Nursing, 33(4), E1-19. doi:10.1097/NCC.0b013e3181cb40c0
- Hogan, R. (2009). Implementation of an oral care protocol and it's effects on oral mucositis. Journal of Pediatric Oncology Nursing, 26(3), 125-135.
- National Cancer Institute (US). Oral mucositis chemoradiotherapy and hematopoietic stem cell transplantation patients management of mucositis accessed on line 3/04/16. http://www.cancer.gov/cancertopics/pdq/supportivecare/oralcomplications/HealthProfessional/page5#Section_85 ; 2013.
- O'Grady et al. (2011). CDC's Guidelines for the Prevention of Intravascular Catheter-Related Infections.
- Peterson DE, Boers-Doets CB, Bensadoun R, Herrsted J, on behalf of the ESMO Guidelines Commitee. Managent of oral and gastrointestinal mucosal injury: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow up. Annals of Oncology 26(Supplement 5): v139-v151, 2015
- Quinn B..UK Oral Mucositis in Cancer Group. (2013). Mouth care guidance and support in cancer and palliative care. London, UK:
- Qutob A.F. et al. Prevention of oral mucositis in children receiving cancer therapy: A systematic review and evidence-based analysis. Oral Oncology 49 (2013) 102–107
- Rubenstein EB et al; Mucositis Study Section of the Multinational Association for Supportive Care in Cancer; International Society for Oral Oncology. "Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis". Cancer. 2004 May 1;100(9 Suppl):2026-46
- Sieracki, R.L., Voelz, L.M., Johannik, T.M., Kopaczewski, D.M., & Hubert, K. (2009). Development and implementation of an oral care protocol for patients with cancer. Clinical Journal of Oncology Nursing, 13(6), 718-722.
- Stephen t. Sonis, dmd, dmsc *oral mucositis in cancer therapy*. Volume 2, supplement 3 ■ November/December 2004
- Van Sebille, Y., Stansborough, R., Wardill, H., et al 2015. *Management of Mucositis During Chemotherapy: From Pathophysiology to Pragmatic Therapeutics.* Current Oncology Reports: 17:50

Vomiting & Nausea

Early and acute complications in BMT setting, diagnosis and management:

- **Management of mucositis & oral care, nausea, vomiting and pain management**
- **Central venous access devices (care of CVAD: Hickman, port and PICC)**
- **Neutropenic fever, management of thrombocytopenia and bleeding**

Definition

Nausea: subjective urge to vomit.

Retching: labored movement of thoracic and abdominal muscles before vomiting.

Vomiting: forceful expulsion of gastric contents coordinated by the emetic center.

CINV – Chemiotherapy - Induced Nausea and Vomiting

Chemotherapy acts on the chemotherapy trigger zone in the brainstem, activating the vomiting center, increasing efferent output to target organs in the gastrointestinal tract resulting in emesis.

Chemotherapy also acts to cause cell damage in the GI tract, resulting in the release of neuroactive agents and vagal stimulation, increasing afferent input to the chemotherapy trigger zone and the vomiting center in the brainstem.

M E Trigg and D M Inverso 2008

CINV classificantion

Acute emesis:

- Occurs within minutes to 24 hour after drug administration.
- Intensity generally peaks after 5-6 hours.
- Usually resolves within the 1° 24 hours.
- Stimulation of neuroreceptors.

Delayed emesis:

- Occurring up to 120 hours after the administration chemotherapy.
- Peak after 3 days.
- May last up to 7 days after chemo administration.
- Exact mechanism unclear:
  - Direct action.
  - Rebound Effetc.
- "Early control".

CINV classificantion

Anticipatory nausea:

- Occurs before chemotherapy administration.
- Conditioned reflex.
- History of anxiety or depressive disorder.
- Poor control with prior cycles.
- After nausea and/or vomiting with previous treatment.
- Trigger by taste odor, memories, visions related to administration of chemotherapy.

Refractory emesis:

- Occurs during subsequent treatment cycles in cases where prophylaxis and/or rescue has failed in early cycles

Causes

Patient-related factor (Causes)

- Females > males.
- Pregnancy-induced N/V.
- Age < 50 yr.
- Previous experiences of nausea:
  - pregnancy;
  - Motion sickness
  - Anaesthesia;
  - Previous chemotherapy or irradiation.
- Ethanol use.
- Anxiety, Nervousness, Depression.

Treatment-related factor (Causes)

Radiation therapy:

- site, treatment field exposure;
- single vs. fractionated doses;
- total dose;
- current or neoadjuvant chemotherapy.

Drug emetogenic potetial

Dose:

- higer dose increase risk;
- divided doses or longer infusion decrase risk.

CINV in HSCT unit (Causes)

The factors that can cause nausea and vomiting, particularly in patients undergoing HSCT, are manifold:

- Chemotherapy (ablative high doses regimes).
- Anticipatory effects (pre-treated patients).
- TBI.
- HCST type (>allogeneic).
- Antimicrobic prophylaxis.
- Infections.
- GvHD.
- Treatment with narcotics analgesic (mucositis).
- Neutropenia.

Trigg ME, Inverso DM. Bona Marrow Transplant. 2008 ;42(8):501-6

Emetic Risk Groups – Adults: Single IV Agents

HIGH	Anthracycline/cyclophosphamide combination* Carmustine Cisplatin Cyclophosphamide ≥ 1500 mg/m² Dacarbazine Mechlorethamine Streptozocin		
MODERATE	Alemtuzumab Azacitidine Bendamustine Carboplatin Clofarabine Cyclophosphamide < 1500 mg/m² Cytarabine > 1000 mg/m²	Daunorubicin Doxorubicin Epirubicin Idarubicin Ifosfamide Irinotecan	Oxaliplatin Romidepsin Temozolomide** Thiotepa Trabectedin

* The combination of an anthracycline and cyclophosphamide in patients with breast cancer should be considered highly emetogenic.
** No direct evidence found for temozolomide IV. Classification is based on oral temozolomide, since all sources indicate a similar safety profile.

Prevention - Prophylaxis

- Standard protocols for prevention of CINV
- Relevant for patients risk factors
- Relevant for drug emetogenicity
- Administer at least 30 min prior to start of treatment
- Information to the patient
- CINV diary

Prevention - Prophylaxis

- Eat prior to treatment.
- Encourage favorite food/drinks.
- Cold drink and meals.
- Chewing gum or sugar free pastilles during treatment.
- Fresh air.
- Environment.
- Relaxation and distraction: music, relaxation CD, video/movie.
- Encourage the patient to notify staff of CINV symptoms.
- Be alert to signs and symptoms of CINV in order to take appropriate action.

Prevention and treatment

- Easier to prevent than treat
- Antiemetic therapy should be adjusted for the drug with the highest emetic risk
- Patients must be protected throughout the full period of risk
- Oral and iv formulations have equivalent efficacy

Non-pharmacologic strategies (Prevention & Tratment)

Limit movements

Behavioural therapy:

- Relaxation techniques
- Systematic desensitization
- Hypnosis
- Guided imagery
- Music therapy

Dietary adjustments

Assessment

Timing, frequency, characteristics of symptoms

Physical exam

Laboratory evaluations

Treatment plan

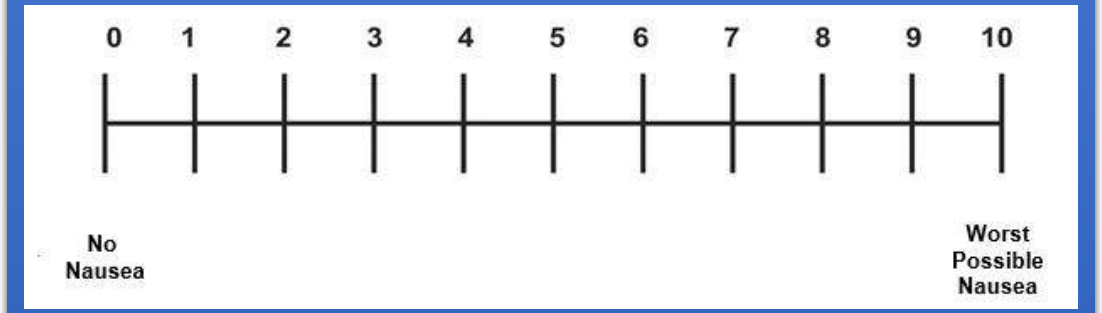
Nusing Assessment

- Check the hydric deficit, monitor weight, skin turgidity, urine concentration and electrolytes.
- Take care of the mouth after each vomiting episode and do mouthwash if necessary.
- Evaluate which foods are preferred and best tolerated
- Encourage eat small and nutritious meals, coordinate the antiemetics administration.
- Avoid fat and spicy foods.
- Encourage drinking liquids and eat light foods.
- Provide intravenous hydration if necessary.

Nausea Evaluations Scales

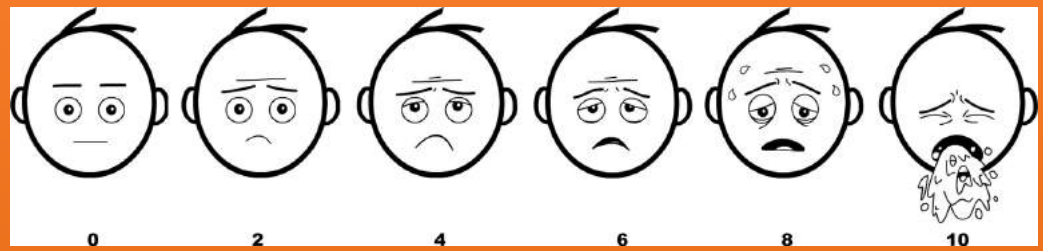
Visual Analogue Scale - VAS

Auto-evaluation scale



Baxter Retching Faces (BARF)

Suitable for children aged 0-7 years



Treatment

Patient Do's and Don'ts:

- Eat smaller, lighter, more frequent meals.
- Avoid high fat and fried foods.
- Dry starchu foods best(crackers, ceral, toast, rice).
- Ice chips, sips of H_20 to prevent dehydratation.
- Keep mouth clear and moist.
- Avoid food preparation.
- Once nausea settles, add variety and increase portion.
- Use a H_2 blocker or PPI to prevent dyspepsia, which can mimic nausea.

Pharmacologic Management

Ideally an Antiemetic should be:

- Available via PO, PR, IV, IM or TD routes.
- Given at least 30-60 min prior to chemotherapy administration.
- Well tolerated.
- Given via the oral route if possible:
  - –Similary effective.
  - –More convenient and less expensive.

Prophylaxis

Pharmacological	
Corticosteroids (Dexamethasone, Metilprednisolone)	
5-HT3-blocker (Dolosetron, Granisetron, Ondansetron, Tropisetron)	Low risk patient Low to medium emetogenicity
Palonosetron	High risk patient Medium and high emetogenicity Combine with corticosteroids Can be repeated every other day 3 times Can be combined with metoclopramide Other 5-HT3-blockers contraindicates
NK1 AR (Aprepitant or fosaprepitant)	High emetogenicity Effective in delayed nausea Salvage if previous prophylaxis failed Combine with 5-HT3-blocker and betamethasone Caution if concomitant p o anticoagulant
Lorazepam	If anticipatory CINV

Nurses Frontiers
www.edu-nursesnofrontiers.com
moodle

EBMT
European Society
for Blood and Marrow Transplantation

ACUTE Nausea and Vomiting: SUMMARY

EMETIC RISK GROUP	ANTIEMETICS
High Non-AC	5-HT_3 + DEX + NK_1
High AC	5-HT_3 + DEX + NK_1
Carboplatin	5-HT_3 + DEX + NK_1
Moderate (other than carboplatin)	5-HT_3 + DEX
Low	5-HT_3 or DEX or DOP
Minimal	No routine prophylaxis

MASCC Multinational Association of Supportive Care in Cancer WWW.MASCC.ORG

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE
European Society for Medical Oncology

5-HT_3 = serotonin$_3$ receptor antagonist

DEX = DEXAMETHASONE

NK_1 = neurokinin$_1$ receptor antagonist such as APREPITANT or FOSAPREPITANT or ROLAPITANT or NEPA (combination of netupitant and palonosetron)

DOP = dopamine receptor antagonist

NOTE: If the NK_1 receptor antagonist is not available for AC chemotherapy, palonosetron is the preferred 5-HT_3 receptor antagonist.

Conclusion

- CINV is preventable in the majority of patients.
- Improvements are still needed in the area of Delayed N/V:
    - Best management → prevention.
- Select the most effective therapy.
- Integrate evidence-based guidelines into clinical practice.

Literature reference

- Lotfi-Jam, K., Carey, M., Jefford, M.,Schofield, P., et al. 2008. NonpharmacologicStrategies for Managing Common Chemotherapy Adverse Effects: A Systematic Review. J ClinOncol26:5618-5629.
- Gralla,R., Osoba, D., Kris, M., Kirkbride, P., et al1999 Recommendations for the Use of Antiemetics: Evidence-Based, Clinical Practice Guidelines. Journal of Clinical Oncology, Vol17, N. 9 (September), pp 2971-2994.
- Multinational Association of Supportive Care in Cancer (MASCC) Guidelines https://www.mascc.org/
- European Society for Medical Oncology - ESMO guidelines https://www.esmo.org/

Pain

Early and acute complications in BMT setting, diagnosis and management:

- **Management of mucositis & oral care, nausea, vomiting and pain management**
- **Central venous access devices (care of CVAD: Hickman, port and PICC)**
- **Neutropenic fever, management of thrombocytopenia and bleeding**

Pain

Pain is a common symptom experienced by patients with cancer from diagnosis through survivorship. Whether as a result of disease or a disease-related treatment.

Types:

- Nociceptive: through tissue damage.
- Neuropathic: due to nerve damage.
- Mixed pain: due to tumor invasion of the nerve.

Categories:

- Acute pain (trauma/surgery).
- Chronic pain (lower back pain like spinal metastases).

Background & Introduction

Moderate to severe pain in cancer is common and affects 70-80% of patients with advanced disease.

Pain causes significant physical and psychosocial burners. A uniquely person experience, pain markedly affects the quality of an individual's life, increases vulnerability in an already vulnerable population, and engenders dependence on healthcare providers for access to adequate pain management.

Evidence from studies shows that many patients have troublesome or severe pain and do not get adequate relief.

The 5th Vital Sign!

Topics

- Safe and effective pain management may include pharmacologic and non-pharmacologic measures
- All people with cancer have a right to optimal relief that includes culturally relevant and sensitive pain education, assessment and management.
- Types of pain management and routes of administration are determined based on many patient-specific-factors, requiring access to:
    - Oral.
    - Transdermal.
    - Rectal.
    - Sublingual.
    - Parental.
    - Intramuscular.
    - Intrathecal.

  administration routes to provide combination therapy that is critical to effective pain management.
- Haematology nurses and doctors must adopt pain management as a priority in continuous quality improvement initiatives.

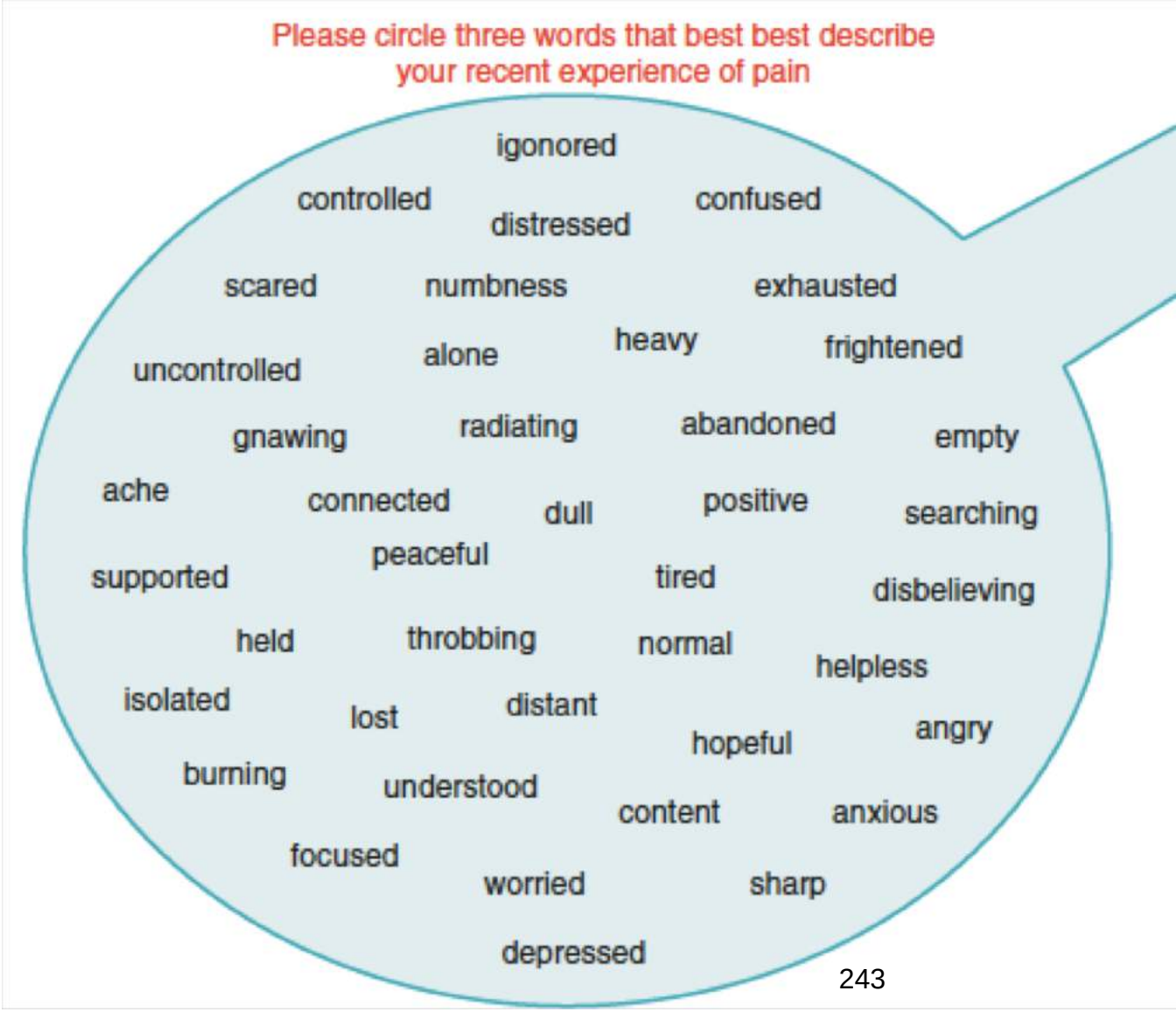
Evidenced based practice & Indications

Measurement

- Self description: self report is the primary source of assessment for people with intact cognitive and verbal skills
- Observation of behaviours
- Physiological parameters

Managing Advanced Cancer Pain Together

Everyone experiences pain differently – you might find it has an impact on your body, on your sense of well-being and how you feel about yourself, and on your relationships with others and the world around you (Managing Advanced Cancer Pain Together – An expert guidance. MACPT (2016). http://macpt.info/)



Scales

Pain assessment

One-dimensional intensity pain scales:

- Visual Analogue Scale (VAS)
- Numerical rating scale (NRS)
- Analog Reports (VRS)

Faces rating scale (FRS)

Behavioral scales

Visual Analogue Scale (VAS)

Instruct the patient to point to the position on the line between the faces to indicate how much pain they are currently feeling. The far left end indicates "no pain" and the far right end indicates "worst pain ever."

Visual Analogue Scale (VAS) – arthritis related
How much pain did you have in the last 7 days? Please pick a point on the given line! no pain ——————————————— worst pain imaginable

Numerical Rating Scale (NRS)

Instruct the patient to choose a number from 0 to 10 that best describes their current pain. 0 would mean "no pain" and 10 would mean "worst possible pain."

Numerical Rating Scale (NRS) – arthritis related

How much pain did you have in the last 7 days?

Please mark the appropriate number!

Verbal Rating Scale (VRS)

The VRS consists of a list of adjectives describing different levels of pain intensity.

An adequate VRS of pain intensity should include adjectives that reflect the extremes of this dimension; from 'no pain' to 'extremely intense pain' and sufficient additional adjectives to capture gradations of pain intensity that may be experienced between these two extremes.

Patients are asked to read over the list of adjectives and select the word or phrase that best describes their level of pain on the scale.

Verbal Rating Scale (VRS) – arthritis related

How much pain did you have in the last 7 days?

Please mark the appropriate statement!

no pain	slight pain	moderate pain	severe pain	worst pain imaginable
☐	☐	☐	☐	☐

FLACC (paediatric)

2 months - 7 years

Assess pain for children betw
een the ages of 2 months and 7 years or individuals that are unable to communicate their pain.

The scale is scored in a range of 0–10 with 0 representing no pain. The scale has five criteria, which are each assigned a score of 0, 1 or 2.

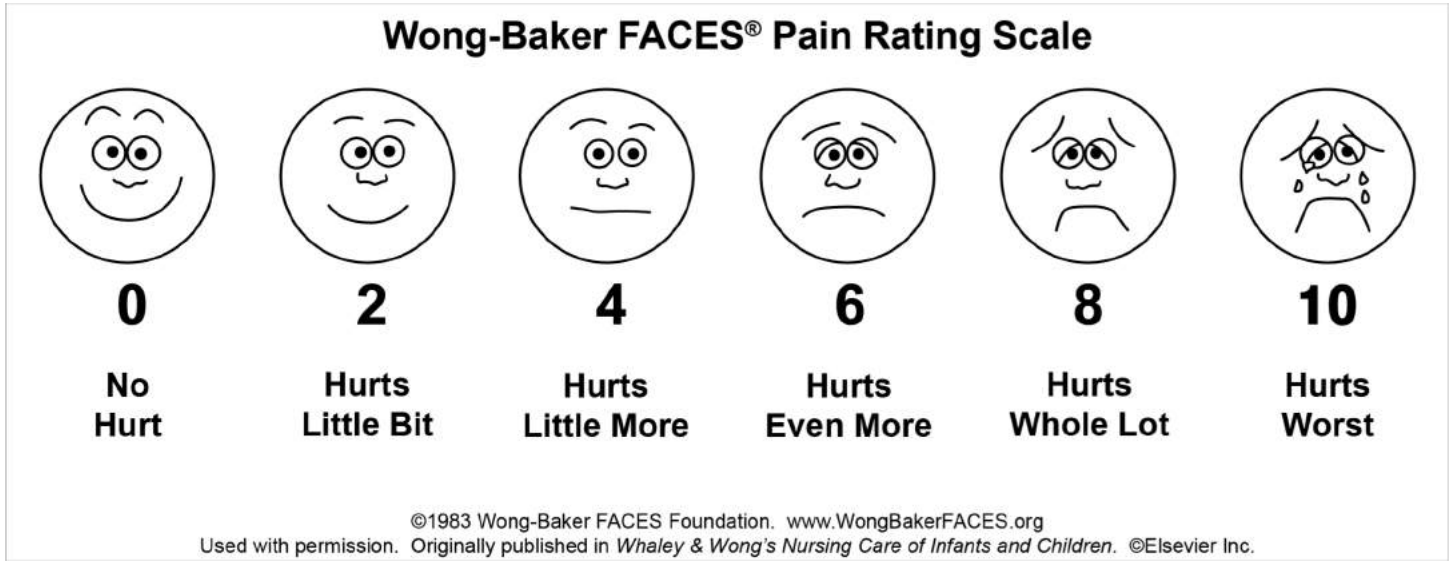
FLACC Scale[2]	0	1	2
1 Face	No particular expression or smile.	Occasional grimace or frown, withdrawn, disinterested.	Frequent to constant frown, clenched jaw, quivering chin.
2 Legs	Normal position or relaxed.	Uneasy, restless, tense.	Kicking, or legs drawn up.
3 Activity	Lying quietly, normal position, moves easily.	Squirming, shifting back and forth, tense.	Arched, rigid or jerking.
4 Cry	No crying (awake or asleep).	Moans or whimpers; occasional complaint.	Crying steadily, screams or sobs, frequent complaints.
5 Consolability	Content, relaxed.	Reassured by occasional touching, hugging or being talked to, distractible.	Difficult to console or comfort.

Scale *Faces Pain Scale*

Wong-Baker 3-8 years

Faces rating scale (FRS)

Adults who have difficulty using the numbers on the visual/numerical rating scales can be assisted with the use of the 6 facial expressions suggesting various pain intensities. Ask the patient to choose the face that best describes how they feel. The far left face indicates "no hurt" and the far right face indicates "hurts worst." Document number below the face chosen.



Behavioral rating scale

The behavioral pain assessment scale is designed for use with nonverbal patients unable to provide self-reports of pain.

- Rate each of the 5 measurement categories (0, 1, or 2).
- Add these together.
- Document the total pain score out of 10.

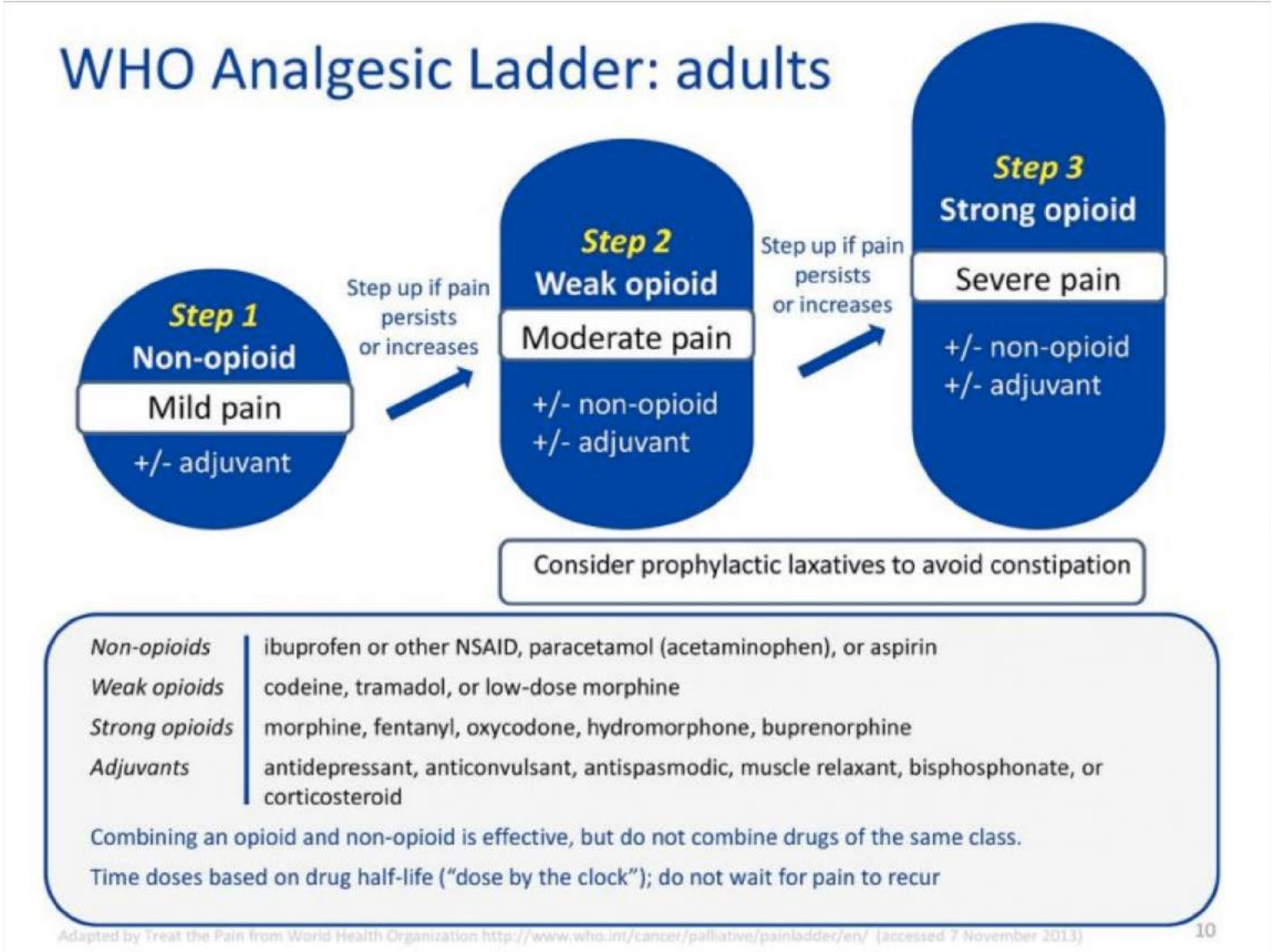
PainAssessmentIN Advanced Dementia" (PAINAD)

For patients unable to provide a self-report of pain: scored 0-10 clinical observation

Face	**0** Face muscles relaxed	**1** Facial muscle tension, frown, grimace	**2** Frequent to constant frown, clenched jaw	**Face score:**
Restlessness	**0** Quiet, relaxed appearance, normal movement	**1** Occasional restless movement, shifting position	**2** Frequent restless movement may include extremities or head	**Restlessness score:**
Muscle tone*	**0** Normal muscle tone	**1** Increased tone, flexion of fingers and toes	**2** Rigid tone	**Muscle tone score:**
Vocalization**	**0** No abnormal sounds	**1** Occasional moans, cries, whimpers and grunts	**2** Frequent or continuous moans, cries, whimpers or grunts	**Vocalization score:**
Consolability	**0** Content, relaxed	**1** Reassured by touch, distractible	**2** Difficult to comfort by touch or talk	**Consolability score:**
Behavioral pain assessment scale total (0-10)				**/10**

***Functional activity score*#**
(Cough/movement)
A – No limitation
B – Mild limitation
C – Severe limitation
#Relative to baseline

* Assess muscle tone in patients with spinal cord lesion or injury at a level above the lesion injury. Assess patients with hemiplegia on the unaffected side.
** This item cannot be measured in patients with artificial airways.


WHO Analgesic Ladder: adults
Step 1
Non-opioid
Mild pain
+/- adjuvant
Step up if pain persists or increases
Step 2
Weak opioid
Moderate pain
+/- non-opioid
+/- adjuvant
Step up if pain persists or increases
Step 3
Strong opioid
Severe pain
+/- non-opioid
+/- adjuvant
Consider prophylactic laxatives to avoid constipation
Non-opioids
ibuprofen or other NSAID, paracetamol (acetaminophen), or aspirin
Weak opioids
codeine, tramadol, or low-dose morphine
Strong opioids
morphine, fentanyl, oxycodone, hydromorphone, buprenorphine
Adjuvants
antidepressant, anticonvulsant, antispasmodic, muscle relaxant, bisphosphonate, or corticosteroid
Combining an opioid and non-opioid is effective, but do not combine drugs of the same class.
Time doses based on drug half-life ("dose by the clock"); do not wait for pain to recur
Adapted by Treat the Pain from World Health Organization http://www.who.int/cancer/palliative/painladder/en/ (accessed 7 November 2013)
10

Drugs administer routes

- Oral
- Percutaneous
- Rectal
- Subcutaneous
- Intramuscular
- Intravenous
- Peridural
- Subaracnoidea

others

Drugs administer in HTCS patients

The administration of non-steroidal anti-inflammatory drugs (i.e. ketoprofen)

could increase the risk of bleeding if platelets level is low.

Nursing interventions

- Information and education.
- Heat.
- Cold.
- Massage.
- Exercise.
- Relaxation.
- Distraction.

Nursing interventions

Heat:

- Indication: reduced transmission of pain signals and relaxation
- Contraindications: acute inflammation, lymphedema, recent radiation, proximity of fentanyl patches
- Method: hot pack, a jug or a hot water bag, a cherry pulp bag heated in the microwave, a hot bath.
- Frequency: Heat is applied at least twice a day at fixed times.

Cold:

- Indication: Cold has a local anaesthetic effect by reducing blood flow and inhibiting inflammatory symptoms pain in combination with inflammation, joint pain.
- Contraindications: Proximity of fentanyl patch, lymphedema, reduced circulation and Raynaud's disease.
- Method: Cold pack or ice cubes. Direct contact should be avoided.
- Frequency: Cold is applied at least twice a day at set times..

Massage:

- Indication: Massage induces a reduced transmission of pain signals and has a local effect as a result of relaxation and improved circulation. Muscle pain due to muscle tension.
- Contraindications: Dermatitis after radiotherapy, inflammation, lymphedema and damage to the skin.
- Method: classical massage applied in the painful area.
- Frequency: Massage is applied at least once a day (but usually more often) at a fixed time

Nursing interventions

Exercise:

- Indication: Exercise therapy can be applied with the aim to improve circulation and to bring about relaxation and improvement of posture and movement.
- Contraindications: Chance of pathological fractures, severe depression, psychosis, oligophrenia and dementia and high fever.
- Method: Active and passive movement promote circulation and lead to relaxation.
- Frequency: Exercise therapy is applied at fixed times at least once a day.

Relaxation:

- Indication: Relaxation techniques bring about a decrease in muscle tension and /or mental tension..
- Method: To achieve relaxation, the following methods are widely used:
    - progressive muscle relaxation (Jacobson method). Characteristic here is the deliberate alternation of muscles to be applied and relaxed;
    - autogenic training (Schulz method). A characteristic feature here is that the patient does not have to do anything, but with the help of instruction on his body to relax;
    - a quiet space is desirable for both methods;
    - relaxation exercises can be combined with focused visualization exercises and meditation;
    - there are bands / CDs with relaxation exercises available. Exercise focused on the specific complaints of the patient usually offers more results.
- Frequency: The patient applies relaxation according to his own insight.

Distraction:

- Indication: When the patient is very occupied by the pain. As an addition to influence the pain experience.
- Method: Rhythmic breathing, singing and rhythmic tapping, actively listening to music are, among other things, forms of conscious distraction.
- Frequency: takes place according to the patient's insight.

Discussion

Monitoring

Patients should be monitored by nurses and the physician.

The purpose is to:

1) Record the data.
2) Evaluate the clinical parameters.
3) Report side effects
4) Implement support therapies

The monitoring of the NRS must take place every 8 hours unless otherwise indicated. After any pharmacological integration with the protocol, the patient should be re-evaluated within one hour.

The aim is to maintain the value of NRS ≤ 3; if higher NRS is detected, administer the drug indicated for Acute Episodic Pain (DEA) and re-evaluate the result after 20-30 'by re-registering the NRS

If it is still high, it is necessary to re-evaluate the pain treatment plan and possibly set up a higher degree of pharmacological protocol.

In patients presenting with nausea and / or vomiting, after having assessed the basic parameters (PA, FC, FR and SaO2) and making sure they are within the norm, administer Metoclopramide 10 mg (in the suspected opioid-related nausea) or Ondansetron 4-8 mg ev (infusion in 100 micrograms in 15 min), this therapy can be repeated up to 4 times in 24 hours.

In patients with continuous infusion of Morfina e.v. it would be good to make a more careful check of the state of sedation and, if the sedation has a score> 4 in the Sedation scale, and / or if the patient has a respiratory rate <10 acts / minute: stop the administration of morphine and evaluate the possibility of administering Naloxone 5 mcg / Kg / ev (1 / 2-1 vial)

Conclusion

The nurse plays a role of primary importance by virtue of the daily contact with the patient that allows him to understand the individual needs.

The continuous updating of the personnel and the correct information of the patient is the basis of the successful outcome of any antalgic therapy.

Literature reference

- American Pain Society –quality of care committee, Quality improvement guide-lines for the treatment of acute pain and cancer pain.
- Kluin-Nelemans JC, Tanasale-Huisman EA. Hematologie. Bohn Stafleu van Loghum. 2013;2:156, 158, 245, 248–9, 253–5.
- Wiskemann J, Huber G. Physical exercise as adjuvant therapy for patients undergoing hematopoietic stem cell transplantation. Bone Marrow Transplant. 2008;41(4):321–9.
- MACPT (Managing Advanced Cancer Pain Together) www.macpt.info

VAD – Vascular Access Devices

Early and acute complications in BMT setting, diagnosis and management:

- **Management of mucositis & oral care, nausea, vomiting and pain management**
- **Central venous access devices (care of CVAD: Hickman, port and PICC)**
- **Neutropenic fever, management of thrombocytopenia and bleeding**

Background & Introduction

- General considerations.
- Type of CVC.
- Risk and complications.
- Preventive and maintenance rules.

Vascular Access – general remarks

Advances in oncology transplant, bedside transfusion medicine, parenteral nutrition, cellular therapy, hemodialysis have been possible by overcoming the inadequacy of peripheral venous access.

The use of central venous catheter (CVC) has many advantages:

- Avoid repeated venipunctures for blood sampling
- Permit the administration of chemotherapy safely
- Permit the administration of hypertonic solution (TPN)
- Permit the administration of blood products (red blood cell transfusion, platelets, fresh frozen plasma, etc.)
- Permit the delivery of intensive high density supportive measures (hyperhydration, blood products, antibiotics, antifungals, antivirals)

Establish an access capable to withstand negative pressure (inlet flow rate up to 100-150 ml/min) and to tolerate the return positive pressure flow rate.

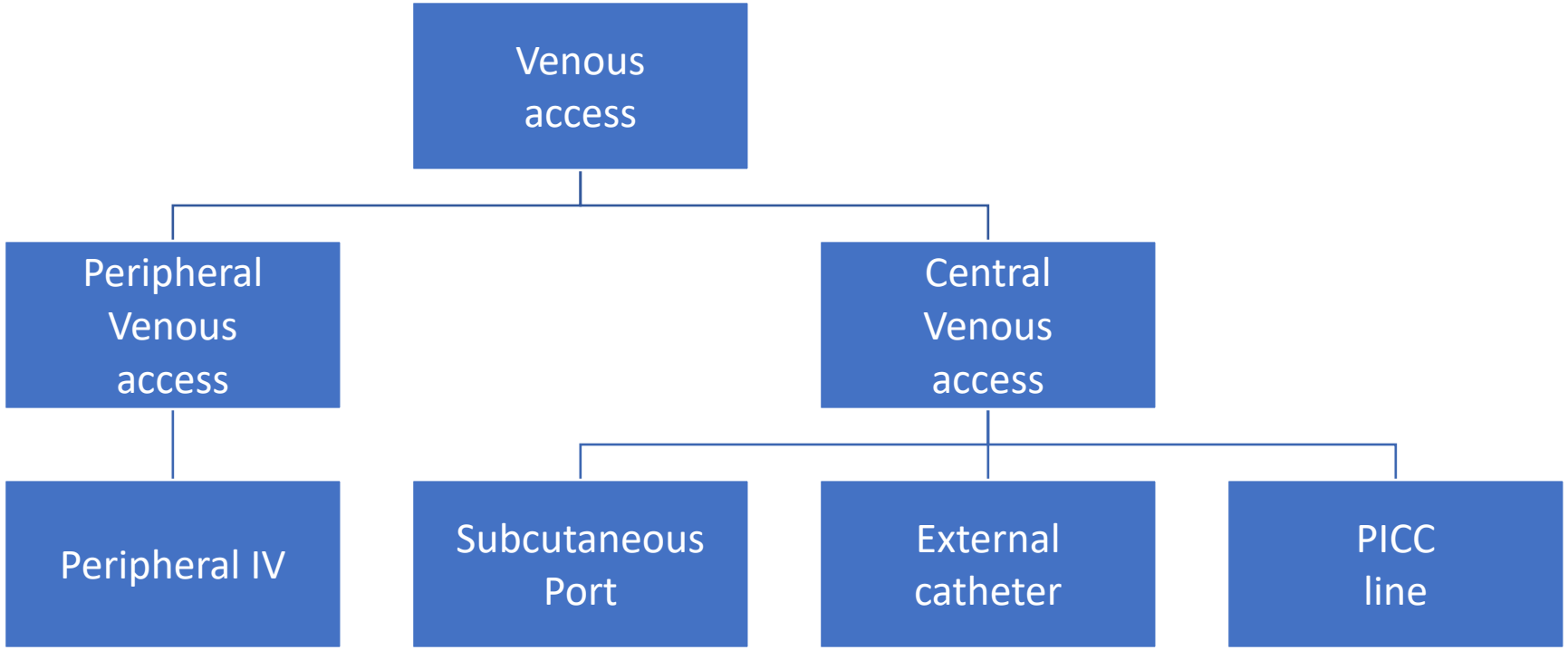
CVC advantages

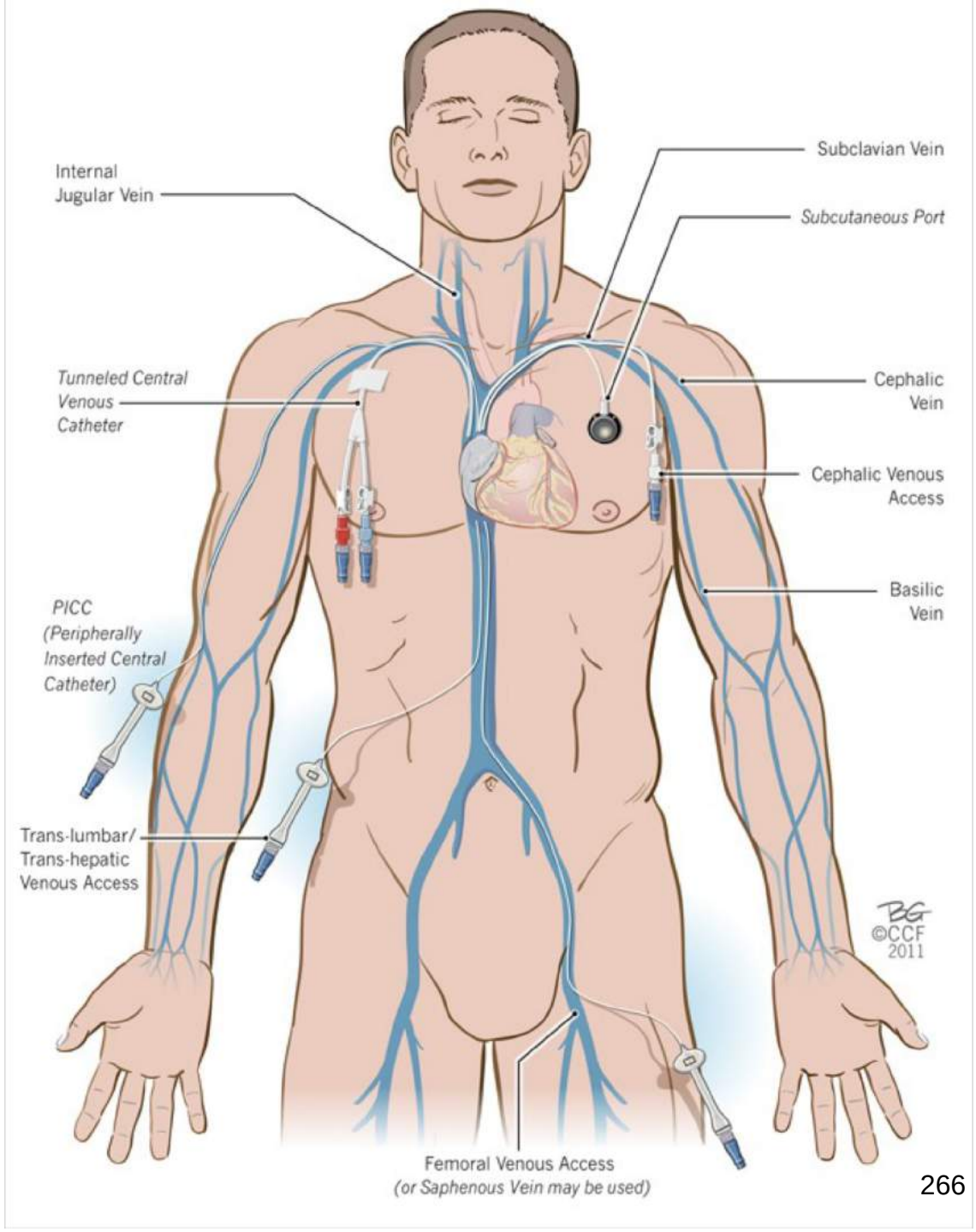
- Easier to access once in place, especially during an emergency.
- Minimizes or eliminates need for repeated venepuncture.
- Increased mobility of patients during infusion.
- Easier to administer treatment as an outpatient.

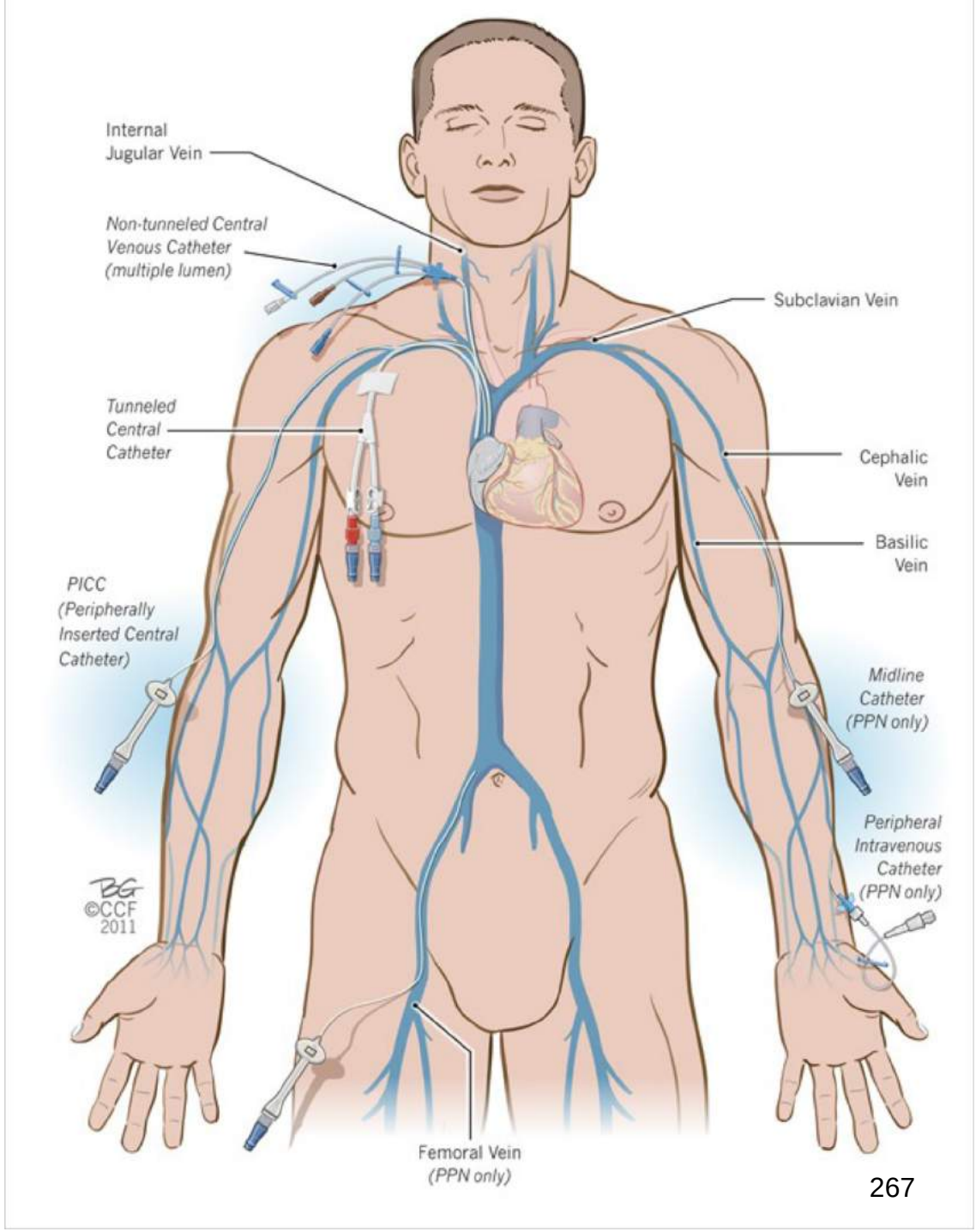
CVC disadvantages

- Surgical procedures for placement:
  - risk associated with surgery, general anaesthesia and complication during insertion
- Requires maintenance.
- Higher risk of infection and thrombotic event.
- Mores expensive.
- Needs of high, updated and adequate professional care.

Types of Venous Access Devices




Internal
Jugular Vein
Subclavian Vein
Subcutaneous Port
Tunneled Central
Venous
Catheter
Cephalic
Vein
Cephalic Venous
Access
Basilic
Vein
PICC
(Peripherally
Inserted Central
Catheter)
Trans-lumbar/
Trans-hepatic
Venous Access
BG
©CCF
2011
Femoral Venous Access
(or Saphenous Vein may be used)


Internal
Jugular Vein
Non-tunneled Central
Venous Catheter
(multiple lumen)
Subclavian Vein
Tunneled
Central
Catheter
Cephalic
Vein
Basilic
Vein
PICC
(Peripherally
Inserted Central
Catheter)
Midline
Catheter
(PPN only)
Peripheral
Intravenous
Catheter
(PPN only)
BG
©CCF
2011
Femoral Vein
(PPN only)

Classification by Permanence

The CVC can be classified according to the permanence time :

SHORT TERM CVC: permanence less than 4 weeks, continuous use, not home use.

MEDIUM TERM CVC: permanence up to 3 months, but also more time, discontinuous use, even at home.

- *Central peripheral insertion catheters (PICC).*
- *Central insertion central catheters (HOHN).*

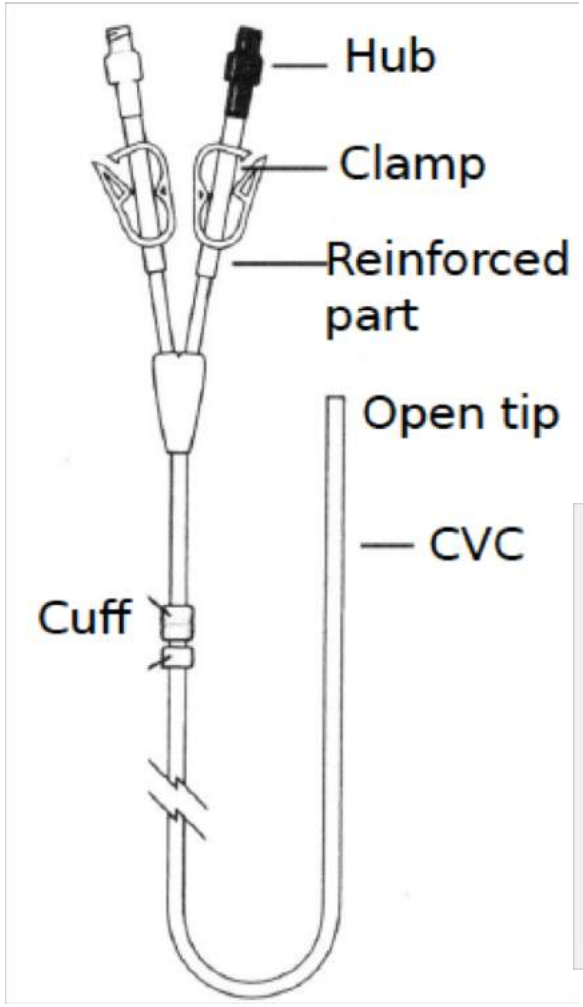
LONG TERM CVC: permanence more than 3 months (discontinuous use).

- *Tunneled catheters (Groshong, Hickman, Broviac).*
- *Total implantable Catheter (Port).*

Type of CVC: Hickman (open tip), Groshong (closed tip)

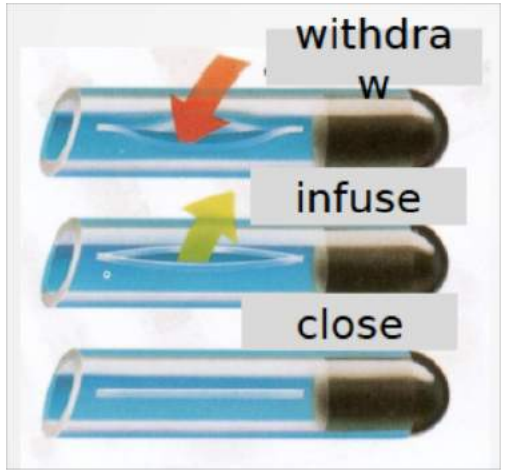
Long term Catherer

Tunnelled, cuffed, catheters made of silicone or other soft plastic material with an external portion of the catheter for access.



Advantages

- Easy to use.
- High flow rate.
- Easy to insert and access.
- Lower incidence of extravasations.
- More often multi-lumen: simultaneous infusions.
- Some mechanical problems can be repaired without replacing catheter.
- Required for BMT.
- Theoretically unlimited lifetime of use.



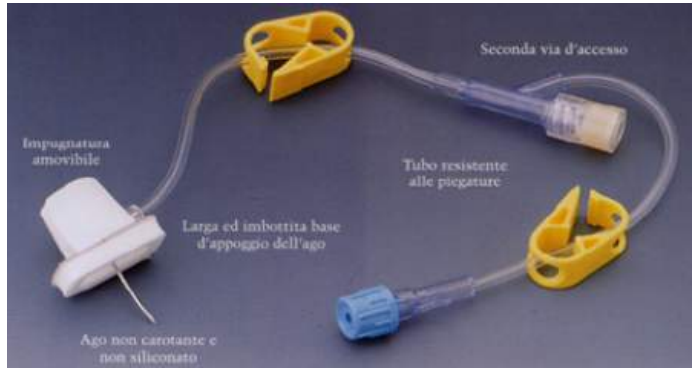
Disadvantages

- Limitation in physical & water activities.
- Altered body image.
- Frequent maintenance.
- Higher incidence of infection.
- Higher incidence of mechanical problems:
- - kink, break or accidental displacement/removal

Type of CVC: PORT

Long term catheter

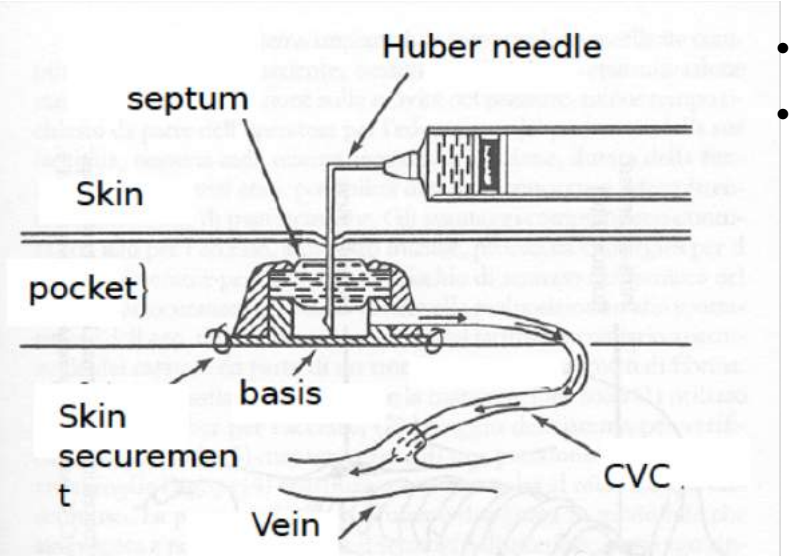
An implanted device surgically placed under the skin.



Advantages

- Limited maintenance.
- Major freedom in physical and water activities.
- Lower incidence of infections.
- Less frequent maintenance and no maintenance required at home.
- Lower incidence of mechanical problems:

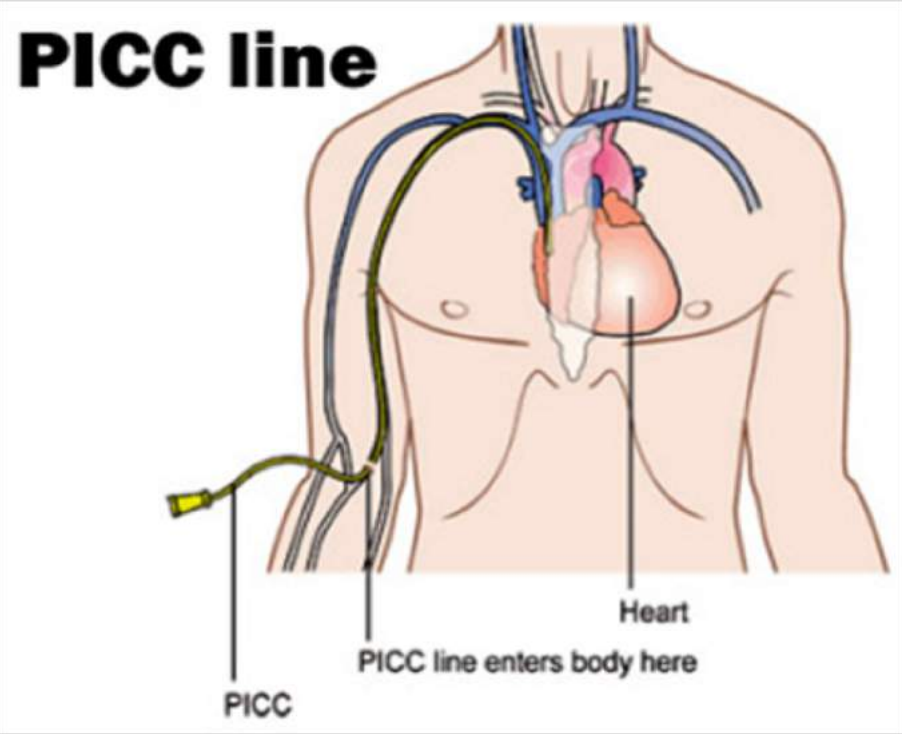
  - catheter kink, break, or accidental removal
- More cosmetically acceptable
- No dressing required



Disadvantages

- Special needle to connect (Huber, Gripper).
- Skin puncture at any connection.
- Not suitable for frequent/continous access.
- Surgical removal.
- Scar after removal.
- Limitation of inlet flow rate.
- More difficult to insert and access.
- Higher risk of extravasations
- More expensive
- Has limited lifetime :
  - approximately 2000 punctures

Type of CVC: PICC



Advantages

- Easy to use, easy to maintain.
- Anesthesia not necessary.
- No risk of arterial or pleural puncture.
- Easy to remove.

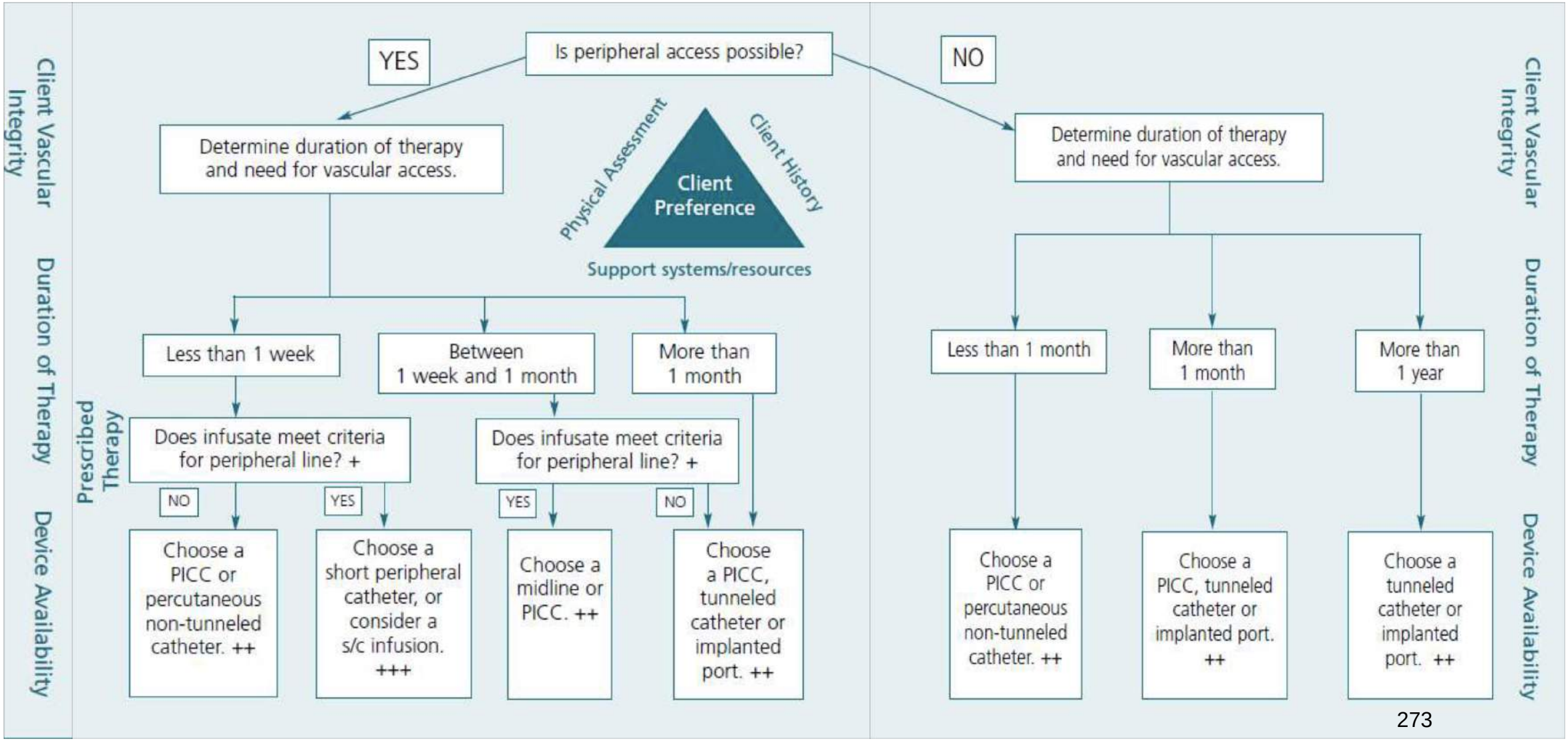
Disadvantages

- Limited duration.
- Smaller lumen.
- More frequent flushing and dressing.
- Higher risk of occlusion/thrombosis and phlebitis.

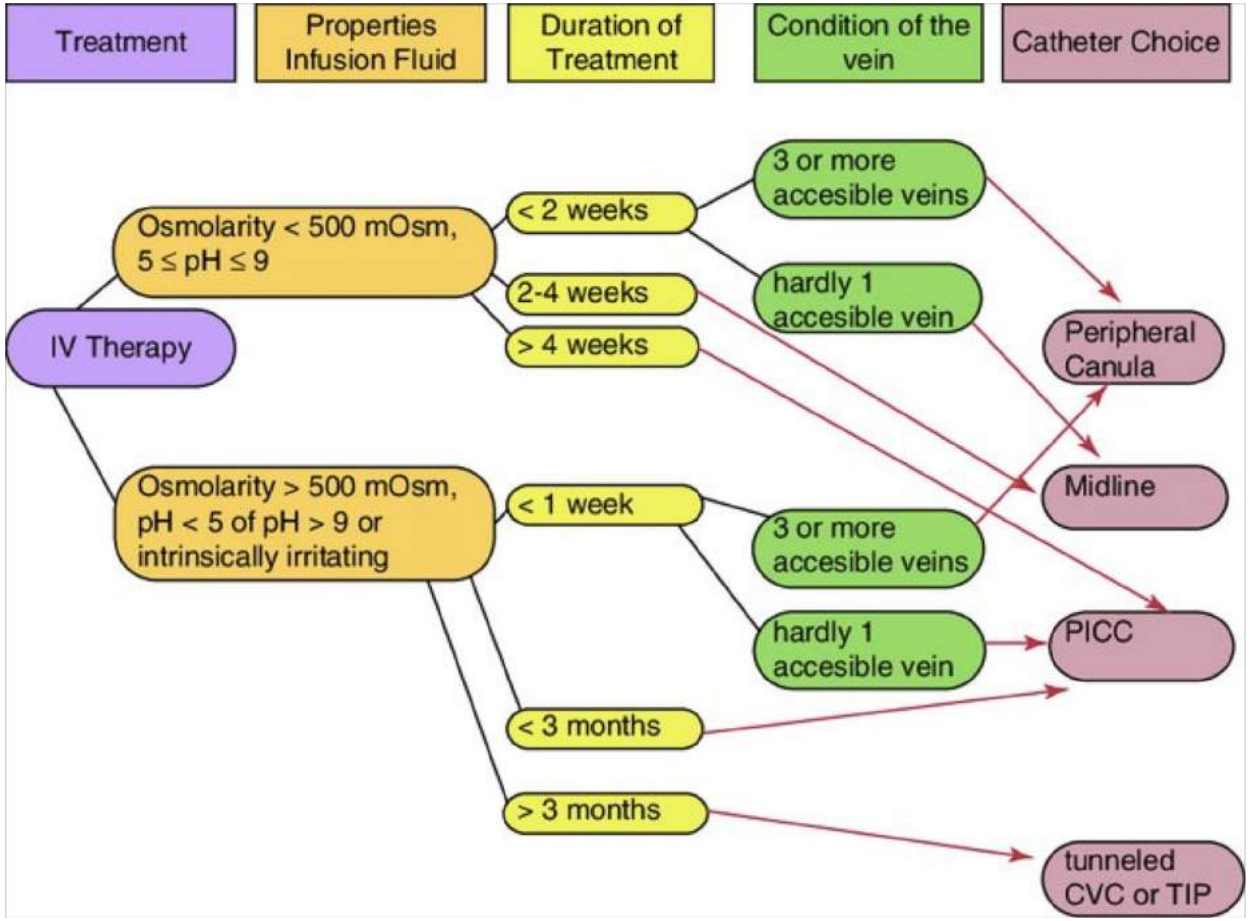
CVC criteria for placement

- Patients has difficult access.
- Long term chemotherapy.
- More of the chemotherapy agents are vesicant agents.
- Need for hyper alimentation.
- Multiple tests blood.

Algorithm CVC criteria for placement



Algorithm intravenous access for non-acute treatment in adults



University Medical Center Utrecht, 2008

Intravascular Access – placement complications

Time	Type	measures
Immediate periprocedural complications	Hematoma, 1-3% Transient arrhythmias Arterial/pleural puncture, 1% Air embolism, 1%	Often self-limiting, purse-string stich , hemostatic dressing Self-limiting, reversal medications US guide, manual pressure for 10 min Always flushing CVC used for placement, left lateral decubitus
Early complication (by day 30)	Exit site infection Tunnel or pocket infection Malfunction	Medication, antibiotics Removal CVC Chest X-ray for malpositioning/displacement, kinking, rupture
Late complications (> 30 days)	Venous stenosis	

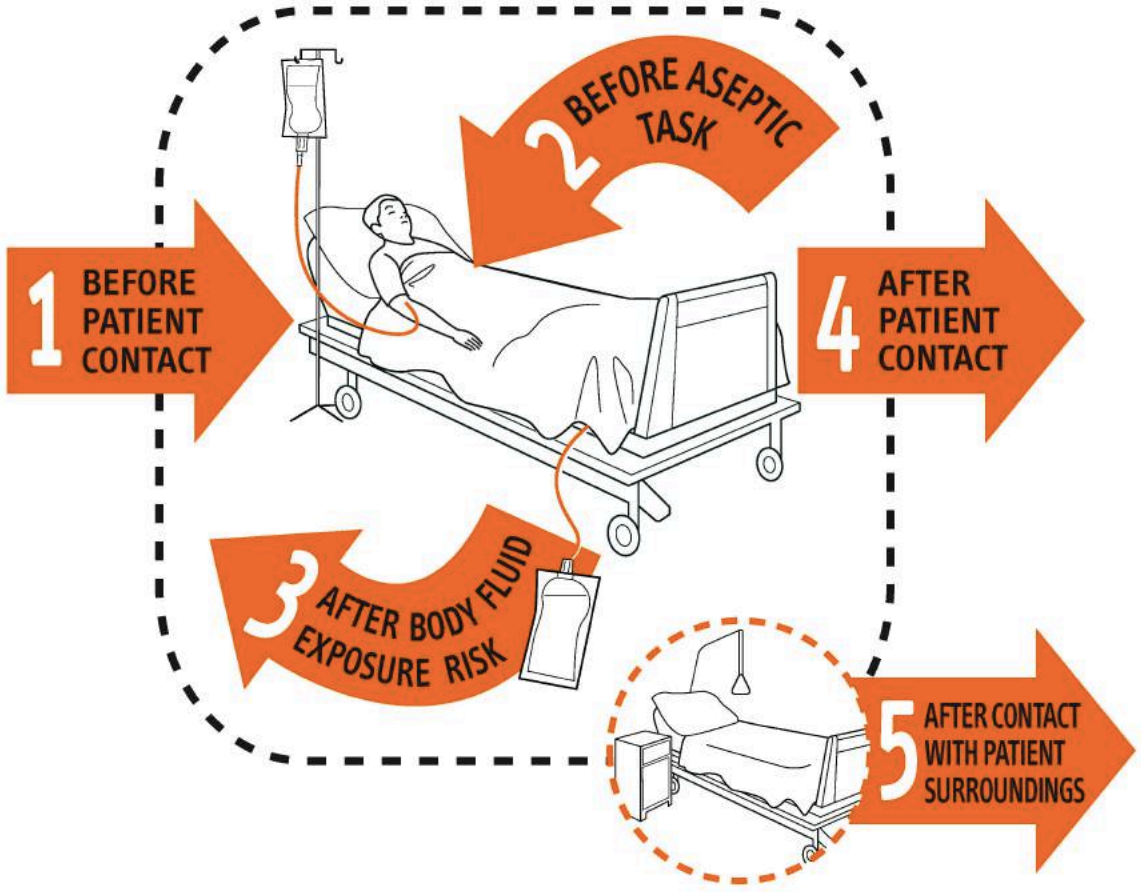
Evidenced based practice & Indications

Perform hand hygiene with before the implant and **before and after ever access to the cvc.**

Perform hand hygiene before and after examining the site.

CVC - Evidence based practice & Indications

Your 5 moments for HAND HYGIENE



1 BEFORE PATIENT CONTACT	**WHEN?** Clean your hands before touching a patient when approaching him or her **WHY?** To protect the patient against harmful germs carried on your hands
2 BEFORE AN ASEPTIC TASK	**WHEN?** Clean your hands immediately before any aseptic task **WHY?** To protect the patient against harmful germs, including the patient's own germs, entering his or her body
3 AFTER BODY FLUID EXPOSURE RISK	**WHEN?** Clean your hands immediately after an exposure risk to body fluids (and after glove removal) **WHY?** To protect yourself and the health-care environment from harmful patient germs
4 AFTER PATIENT CONTACT	**WHEN?** Clean your hands after touching a patient and his or her immediate surroundings when leaving **WHY?** To protect yourself and the health-care environment from harmful patient germs
5 AFTER CONTACT WITH PATIENT SURROUNDINGS	**WHEN?** Clean your hands after touching any object or furniture in the patient's immediate surroundings, when leaving - even without touching the patient **WHY?** To protect yourself and the health-care environment from harmful patient germs

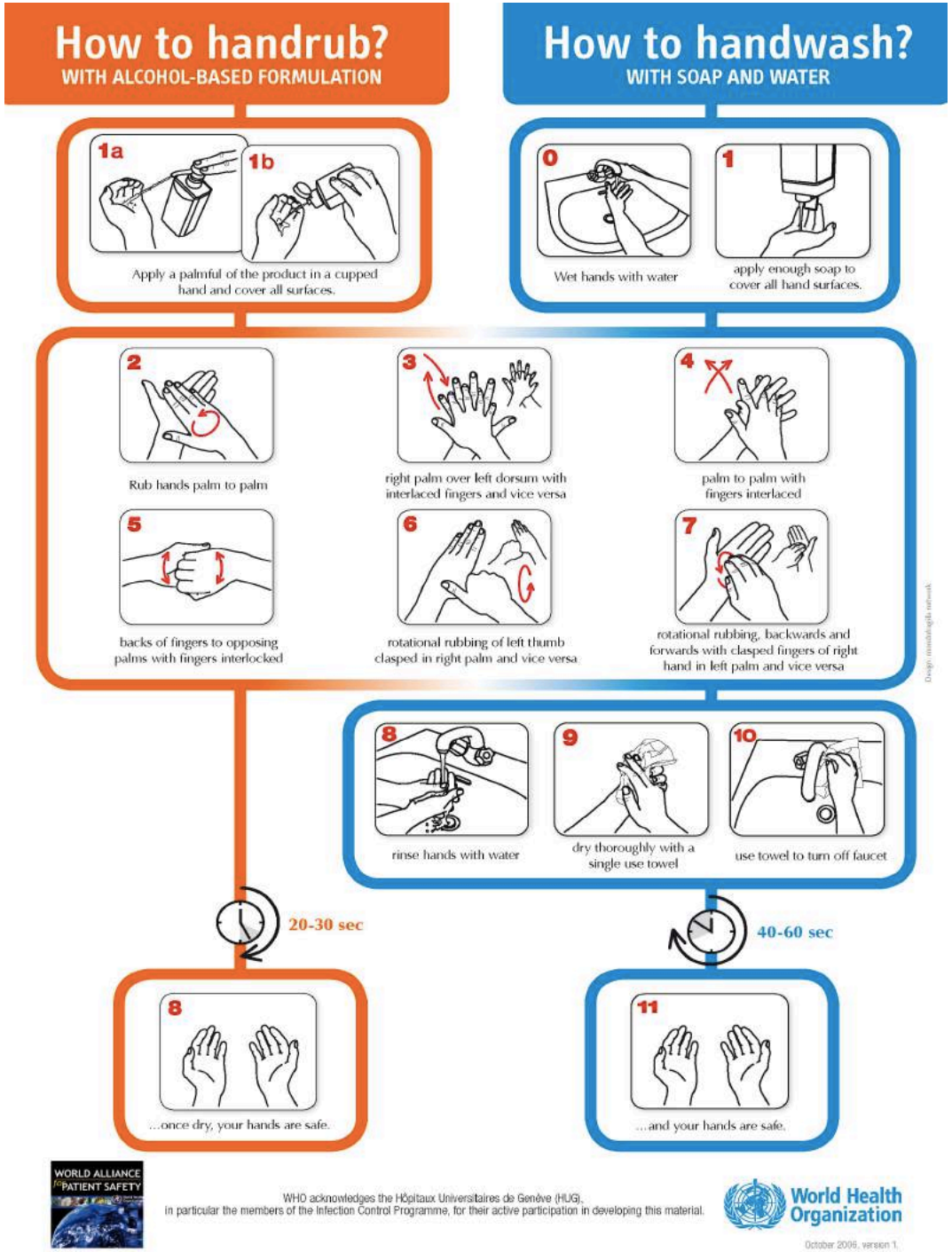
WHO acknowledges the Hôpitaux Universitaires de Genève (HUG),
in particular the members of the Infection Control Programme, for their active participation in developing this material.

World Health Organization

October 2006, version 1.

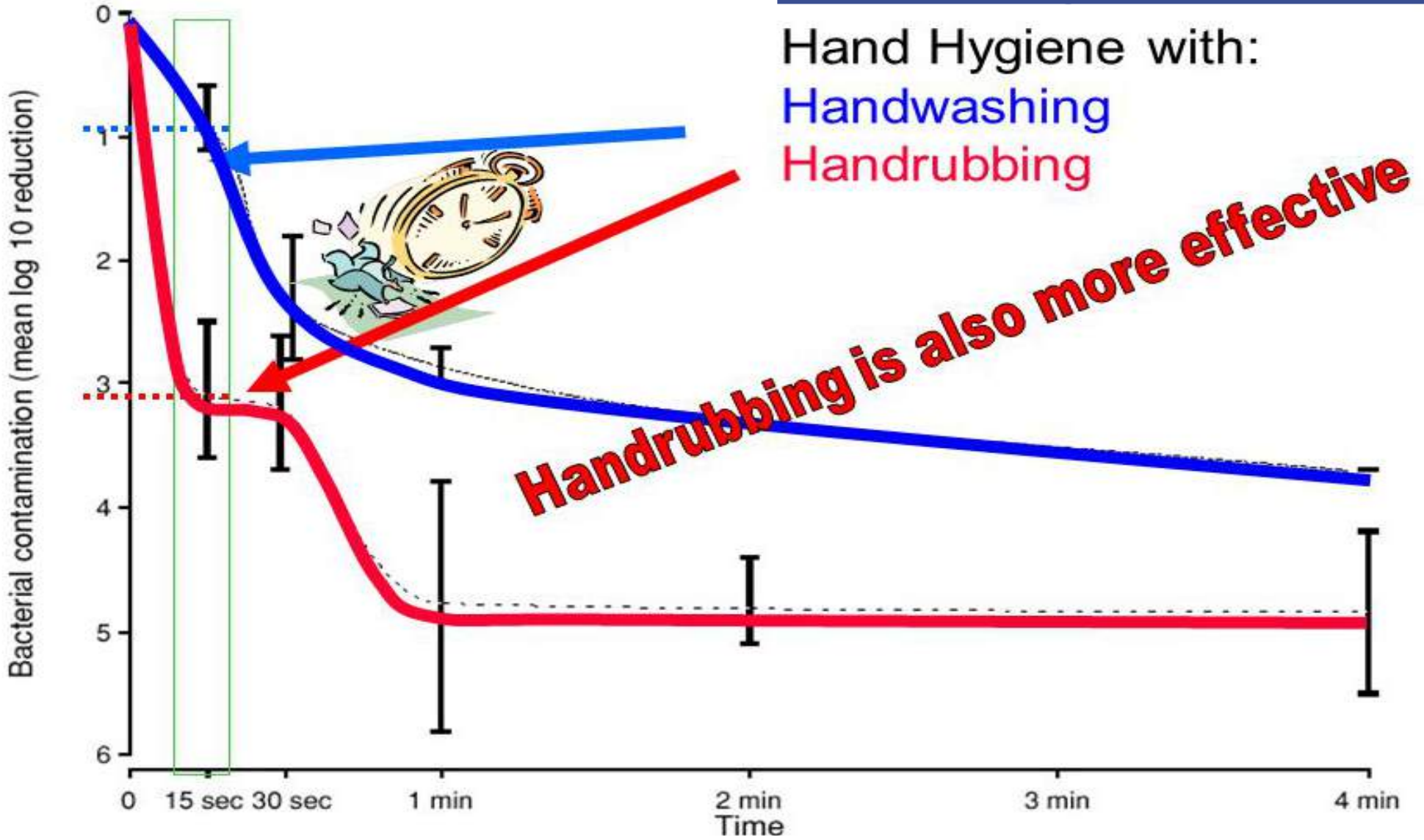
Nurses Frontiers
www.edu-nursesnofrontiers.com
moodle

EBMT
European Society
for Blood and Marrow Transplantation



Application time of Hand Hygiene and reduction of Bacterial Contamination :

Handwashing vs Handrubbing



Dressing Type

Sterile Gauze Dressing

Sterile Semi-permeable Transparent Dressing

Dressing Type

TYPE	CHARACTERISTICS	CHANGING TIME
Sterile Semi-permeable transparent Dressing	• Permit continuous observation around the entire insertion site. • Hypoallergenic. • Waterproof film. • Breathable film allows skin to function normally with good exchange of moisture vapor and oxygen. • Not use on pathological skin.	Change every 7 days or if dirty, detached or wet.

Sterile Gauze Dressing	• Allows movements.
	• First choice when:
	  • Exit-site with presence of exudate, blood and profuse sweating.
	  • Presence of stitches at the exit site.
	  • In the first 25-30 days after placement (in case of tunnelled CVC)
	  • Intolerance to polyurethane dressing.
		Change every 72 hours or
		if dirty, detached or wet.

Is recommended to use aseptic procedure for the exit site dysinfection.

Remember:

- Appropriate frequency of medication.
- Aseptic technique.
- Skin antisepsis with alcoholic chlorhexidine 2%.
- Prefer semi-permeable transparent dressings.
- Chlorhexidine 2%-releasing felt pads.
- Sutureless CVC fixing.

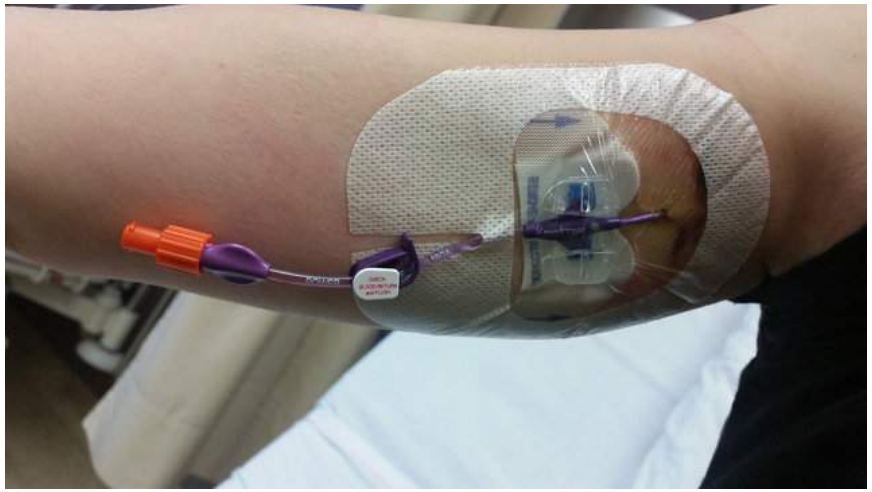
Disinfectant solutions

Alcoholic Chlorhexidine 2%	Povidone-iodine 10%
• More effective than disinfection with iodine-based solution. • Minimum action time 30 seconds. • Do not use on damaged skin.	• Increased compliance. • Use for those patients with an established history of chlorhexidine sensitivity. • Minimum action time 2 minutes.
Not recommended for children younger than 2 months.	

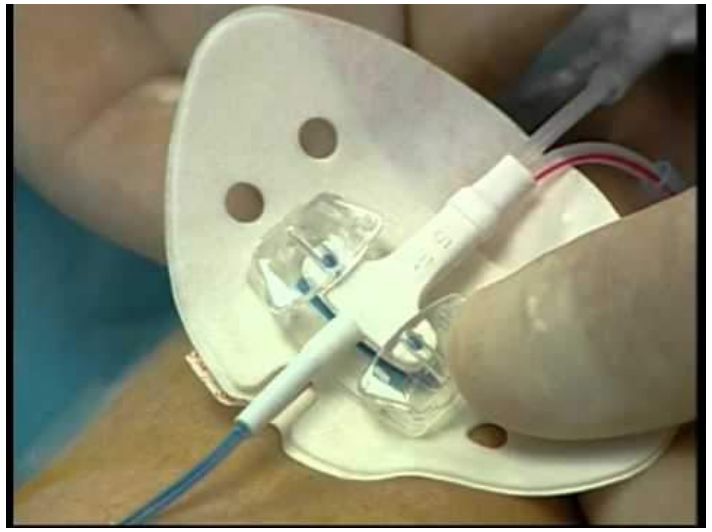
Flushing solution

Author, year, population, CVC type	Type of intervention	Comments
Cesaro (2009), ped, B-H	Heparin 200 UI/ml vs NS + PPD	Higher incidence of CVC occlusion and bacteremia with NS + PPD
Goossens (2013), adult Port	Heparin 100 UI/ml vs NS	No difference between arms
Lopez-Britz (2014), adult, PICC, Port, CVC 2-3 lumen (dialysis, ICU)	Heparin 10-5000UI/ml vs NS	Weak evidence of superiority of heparin for preventing occlusion
Conway (2014), ped, B-H, PICC, Port	Review literature on frequency and type of flushing	Frequency: daily to 1-3 times/week (PICC, B-H) or monthly (Port) Solution: NS or Heparin, weak evidence for using heparin

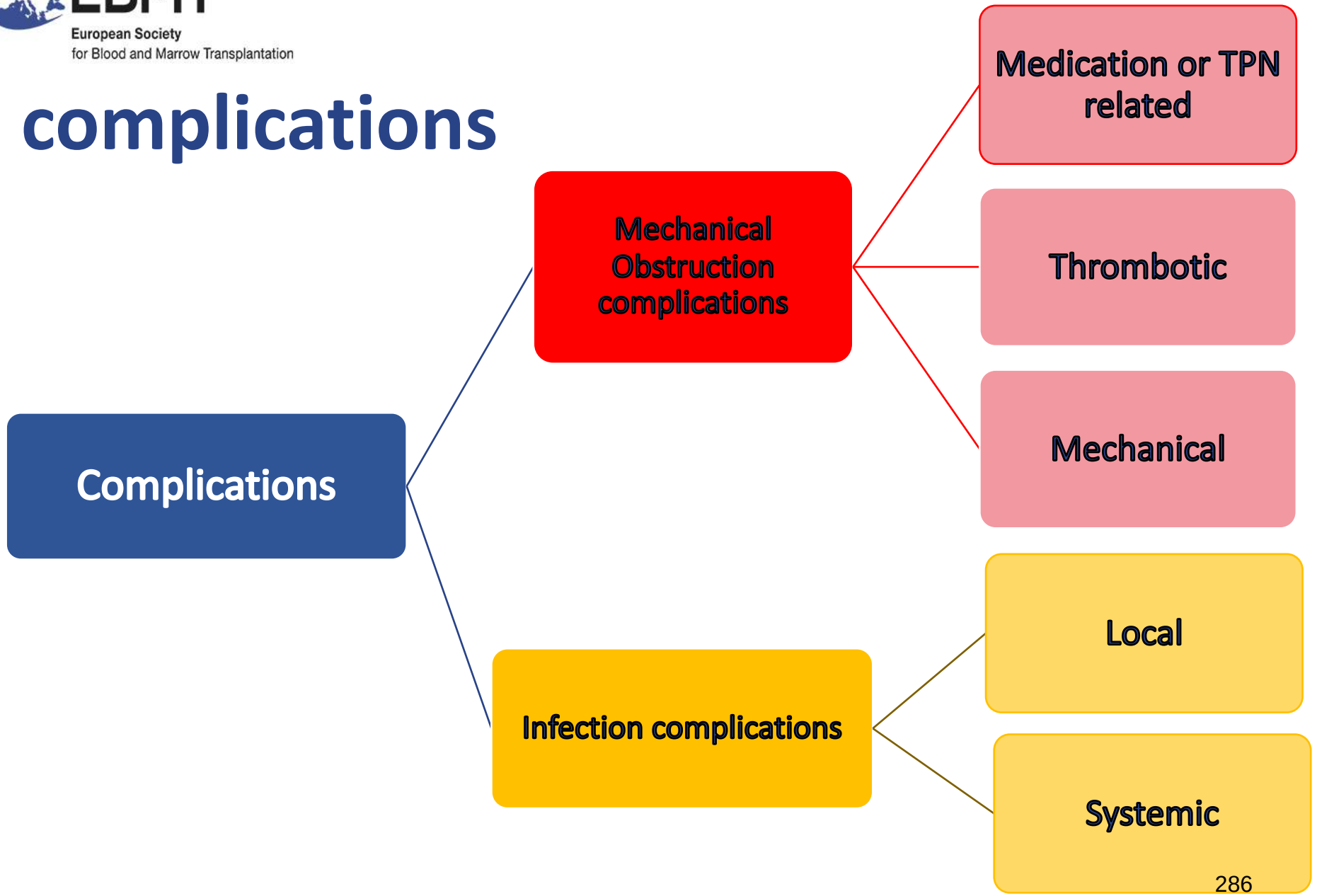
Sutureless devices



The most important recommendations concerning the prevention of CVC-related bloodstream infections include use of sutureless devices for fixing the catheter.



Common complications



Mechanical complications

- Catheter Kink.
- Rupture of catheter.
- Catheter dislodged.
- Extravasations.
- Chamber of port dislodged or cracked.
- Migration of catheter.

Catheter obstruction

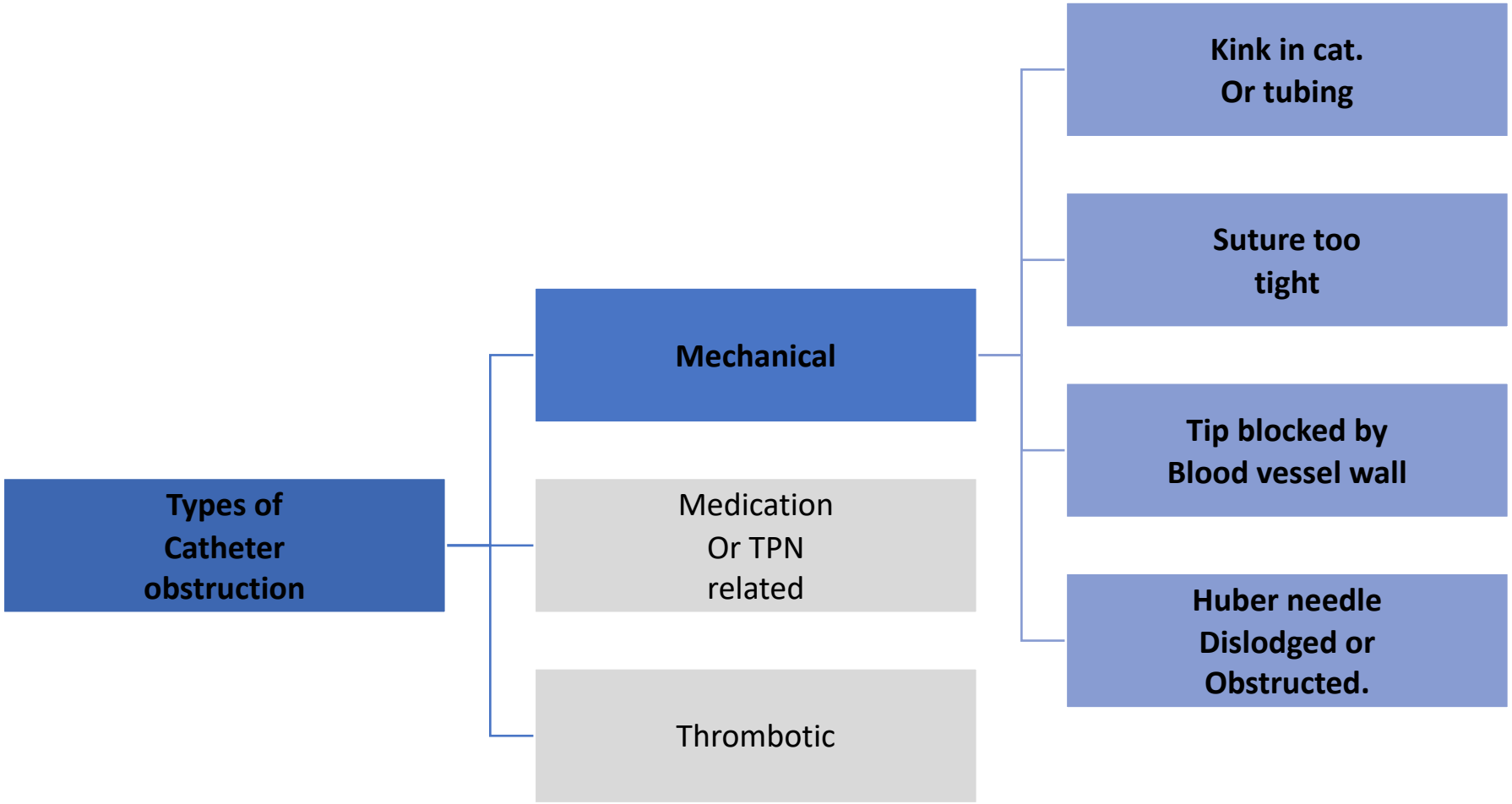
Inability to draw blood and/ or infuse saline through a CVC is the first sign that there is a catheter obstruction.

- **Partial** : cannot withdraw blood, **but** can infuse.
- **Complete**: cannot withdraw blood **or** infuse.

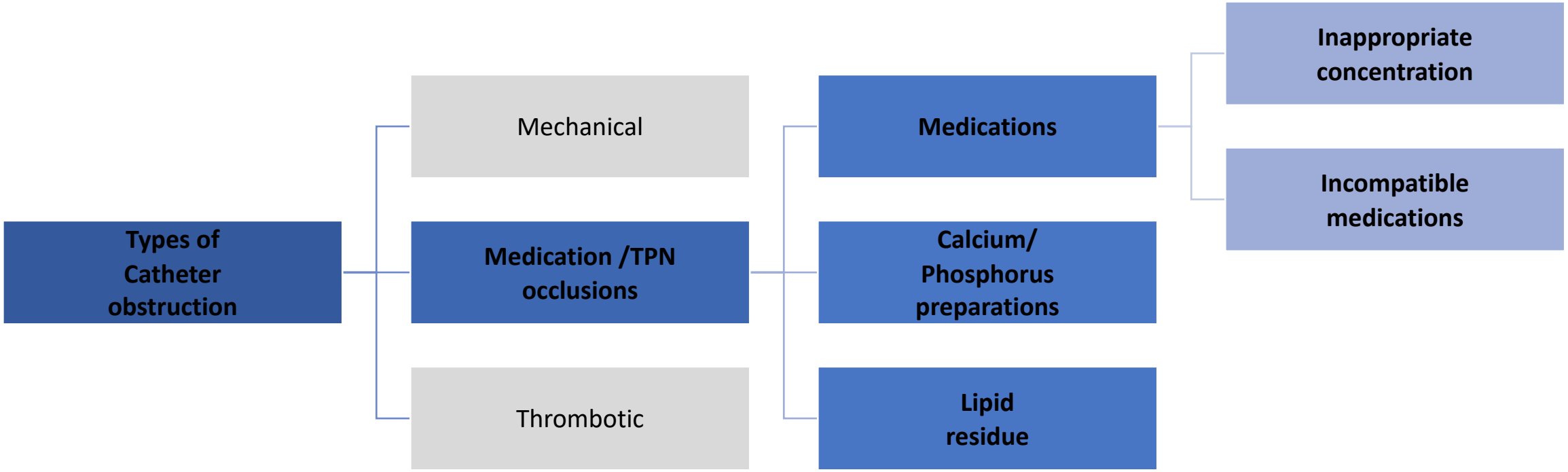
Risks contributing to thrombotic obstruction:

- Inadequate flushing of the catheter
- May allow accumulation of fibrin around the catheter
- Insufficient Heparinization
- Inadequate flow through the catheter
- infusion rate too slow

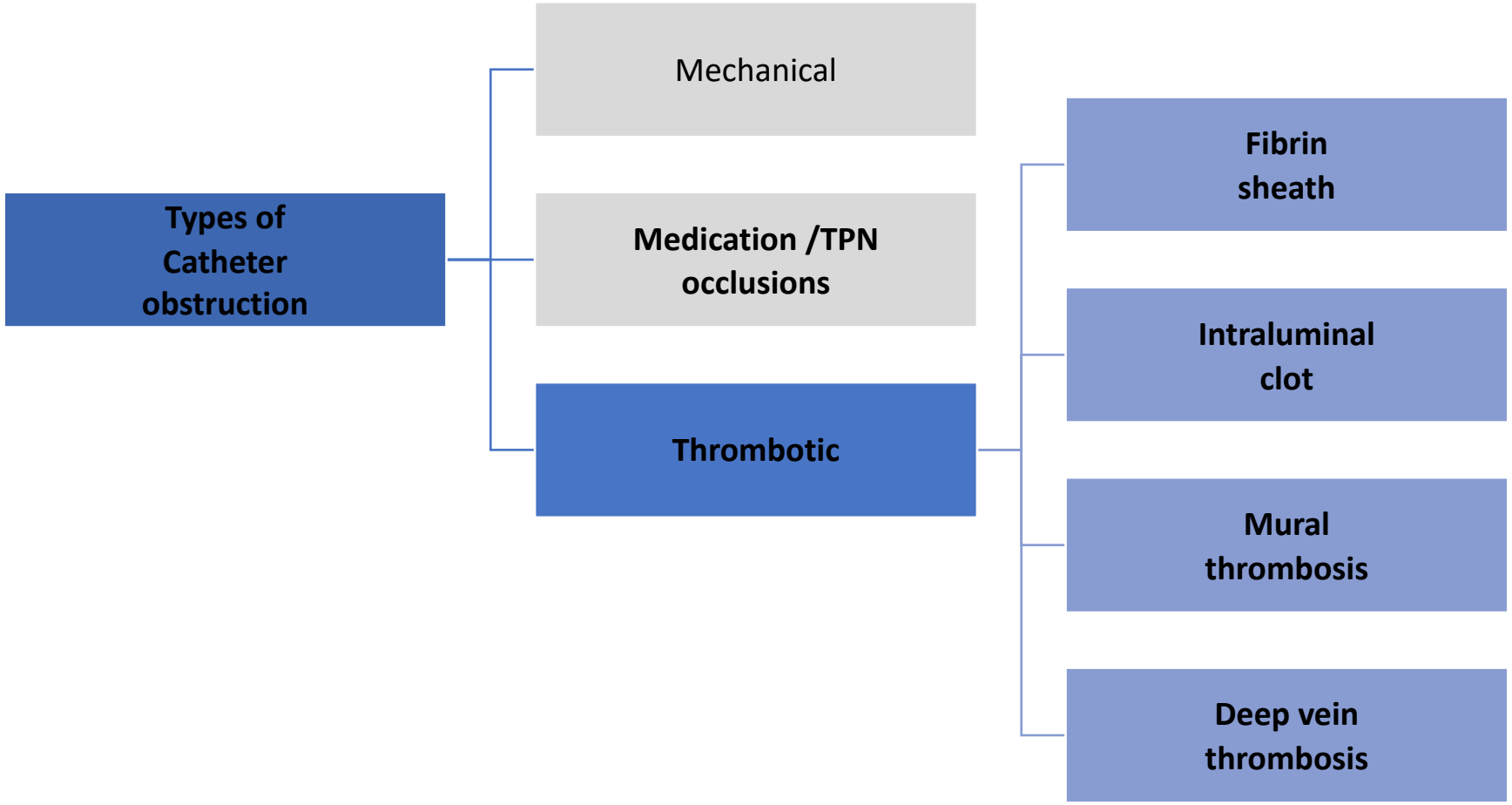
Catheter obstruction



Catheter obstruction

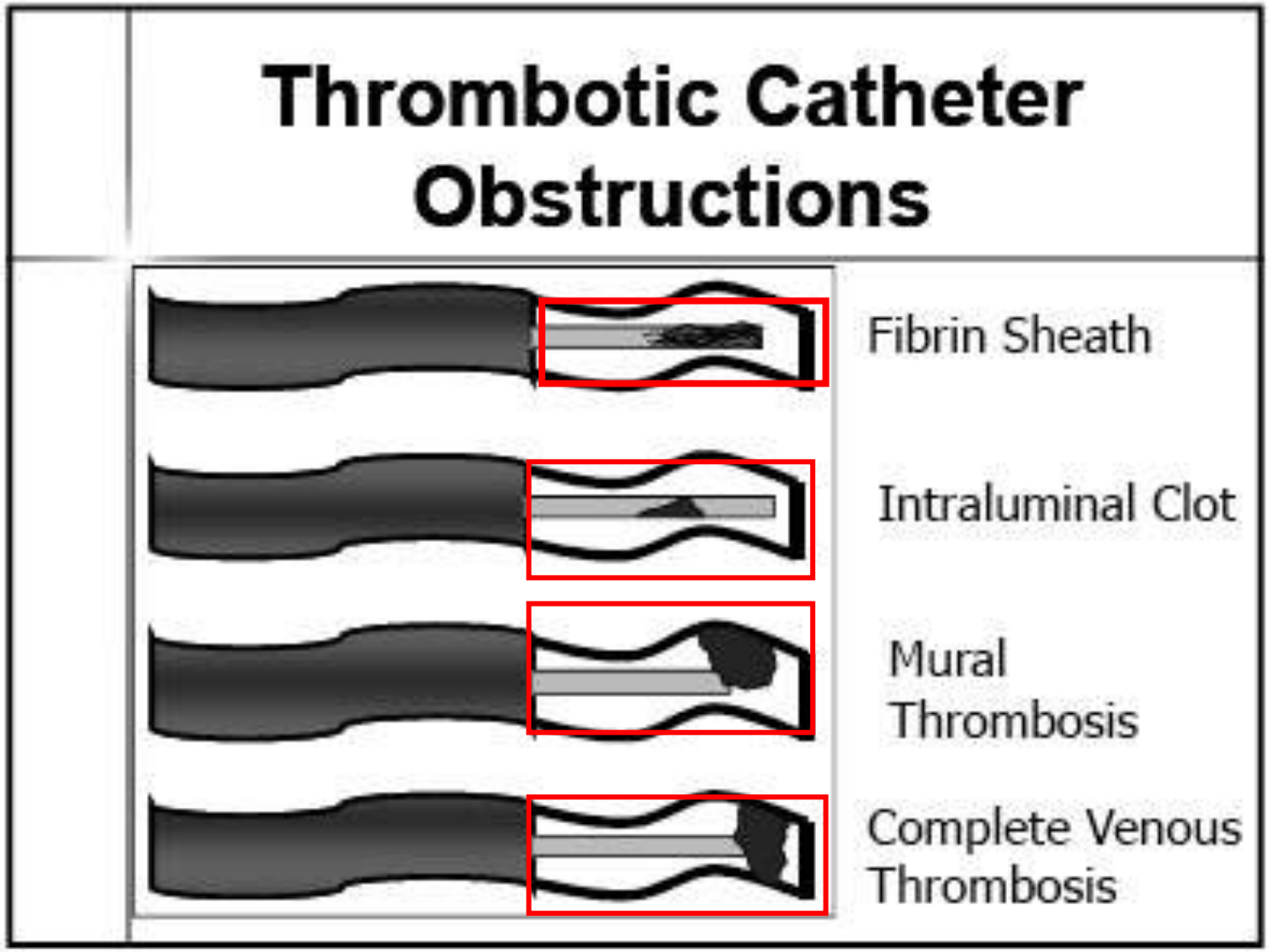


Catheter obstruction



Catheter obstruction

- **Medication**:
  - inappropriate concentration of medications
    - mixing of incompatible med. trough the CVC
      + gradual
      + immediate
- **Calcium/phosphorus**: crystallization often seen with TPN
- **Lipid**: residue from TPN preparations


Thrombotic Catheter Obstructions
Fibrin Sheath
Intraluminal Clot
Mural Thrombosis
Complete Venous Thrombosis

Infectious complications

Types of Catheter Infections:

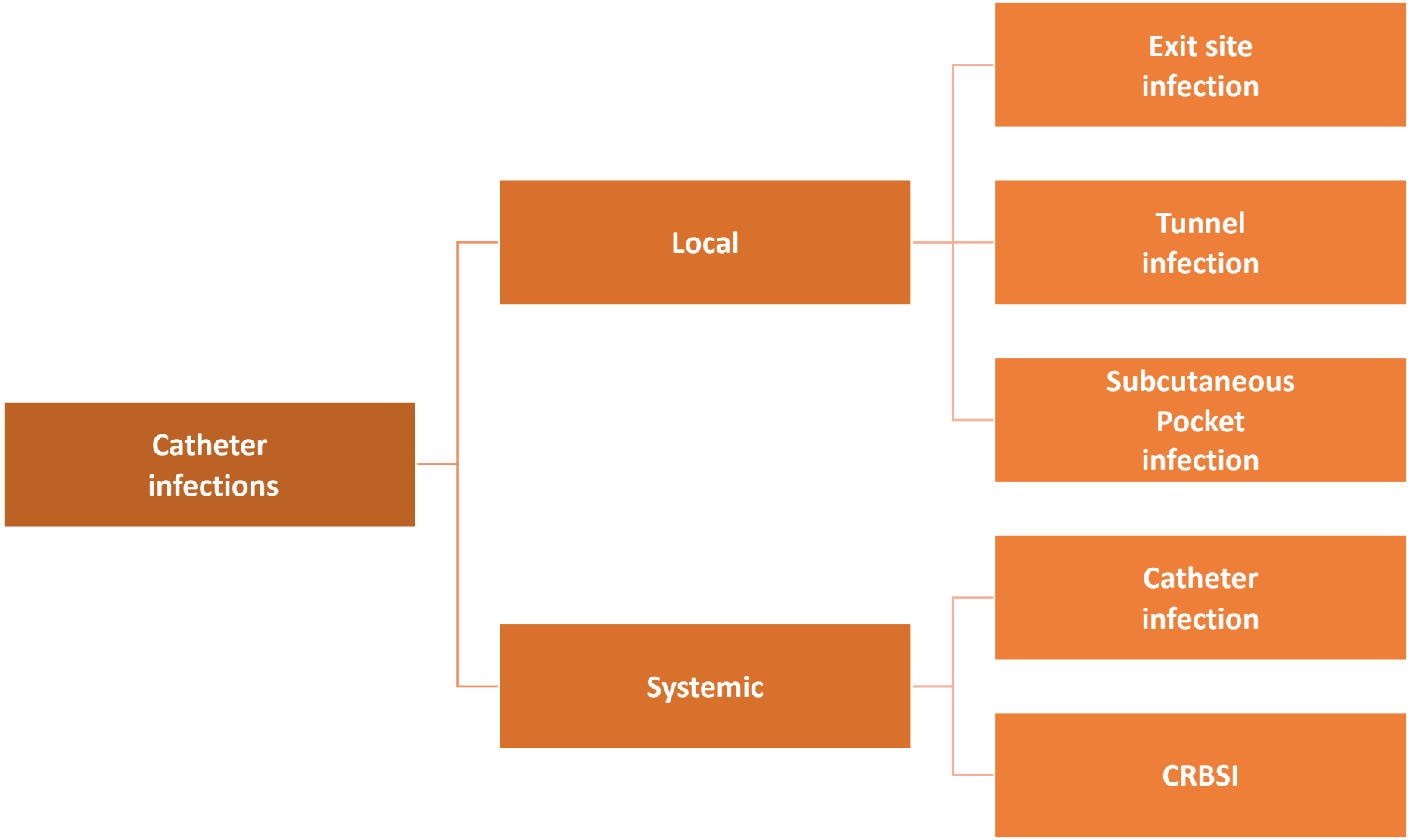
LOCAL:

- Exit site.
- Tunnel.
- Subcutaneous pocket.

SYSTEMIC:

- Catheter related blood stream.
- Infections.
- Septic thrombosis.

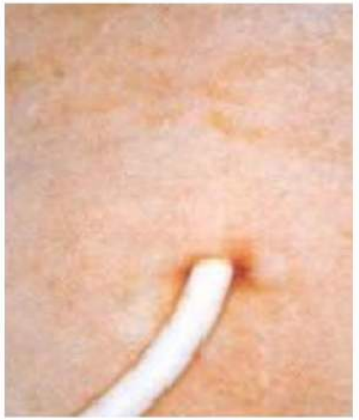
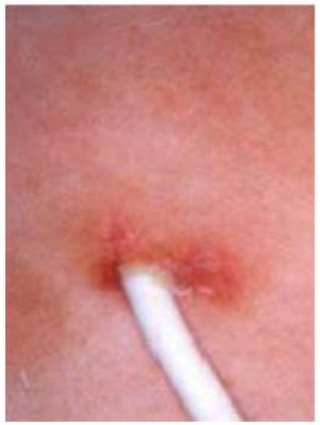
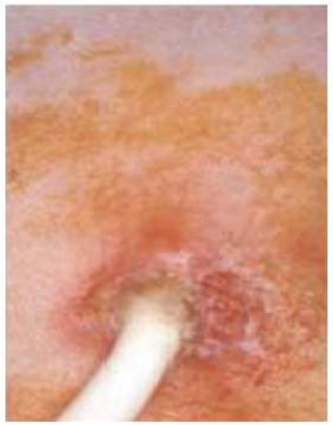
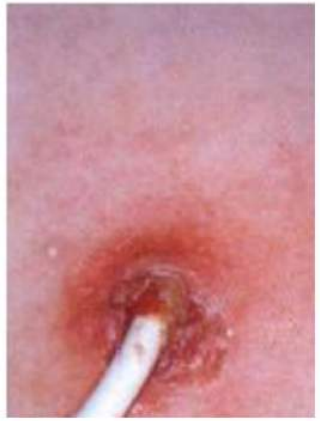
Infectious complications



Risks to develop catheter infection

- Young age: (infants and toddlers)
- External catheter
- Catheter Related Thrombosis
- Leukaemia, Neutropenia, and HSCT
- Increased number of times catheter is accessed
- Poor catheter care.

Manging Exit-site Infection

CVC EXIT SITE SKIN INFECTION SCORE				
SCORE	**0**	**1**	**2**	**3**
				
PAIN	Absent	Absent/Present	Present	Present
SKIN	Intact	Intact	Damaged	Damaged
REDDENING	Absent	<1cm around CVC exit site	>1cm and <2cm around the CVC exit site	Present
FIBRIN	Absent	Absent/Present	Absent/Present	Absent/Present
SECRETION/PUS	Absent	Absent	Absent	Present

Interventions for CVC exit site infection

MANAGEMENT OF CENTRAL VENOUS CATHETER				
SCORE	**0**	**1**	**2**	**3**
DRESSING CHANGING FREQUENCY	Standard CVC dressing change with Chlorhexidine gluconate 2% every 7 days.	Tight CVC dressing change with Chlorhexidine gluconate 2% every 2-3 days.	Tight CVC dressing change with Iodopovidone 10% every 1-2 days.	Tight CVC dressing change with Iodopovidone 10% every 1-2 days.
EXIT SITE SWAB	None.	Yes. Antibiotic treatment*.	Yes. Antibiotic treatment*.	Yes. Antibiotic treatment*. If no improvement CVC removed.

*Rifampicin topical solution or Teicoplanin powder

Castagna A., Grossule M. Adapted from Cesaro S. et al Ann Hematol. 2016; 95:817-25.

Manging CVC luminal Infection

Antibiotic lock therapy

Definition:

- High concentrations of antibiotics locked in lumen of catheter.

Effective:

- Coagulase Negative Staphylococcus infection.

Not effective:

- Local infection.
- Infection that occurs less than 2 weeks after catheter placement.

Infectious complications: SYSTEMIC

Definition:

- Bacterial colonization of the catheter.
- Focus of infection is within the catheter lumen.
- Catheter blood culture = positive.
- Peripheral blood culture = negative.

Signs and Symptoms:

- Fever.
- Swelling, erythema, induration around the catheter.
- Hypotension or chills when catheter is flushed or manipulated.

Catheter related bloodstream infections

- Bloodstream infection that originates from a catheter infection.
- **Treat with broad spectrum antibiotics until sensitivity of culture known.**
- Cover gram (-) and gram (+) bacteria.
- May benefit from Antibiotic lock therapy.
- Especially Coagulase Negative Staph infections, if no response, may need to remove catheter.

Catheter infections: **Complications**

Septic Thrombosis

- Persistent infection + signs of catheter obstruction
- **Treat with prolonged antibiotics and anticoagulation**

Infective Endocarditis

- Persistent infection + cardiac insufficiency
- **Treat with prolonged antibiotic or antifungal therapy**

When to remove the catheter

Local infection:

- Patient deteriorates.
- Infection extends despite IV antibiotics.
- Infection with rapid growing Acid Fast Bacillus.

Catheter Related Bloodstream Infection:

- Persistent fever or persistent (+) Blood cultures.
- Signs of sepsis not responding to therapy.
- Blood cultures positive for resistant organism.
- Recurrent Catheter related blood stream infection.

Conclusion

INFECTION CONTROL

- Aseptic/sterile technique, Standard Precautions, maintain product sterility during all infusion procedures.
- Maximal sterile barrier precautions during insertion .
- Hand hygiene.
- Performance improvement – monitoring of infection control practices to minimize health care acquired (associated) infections, to provide corrective action.
- Use of sutureless devices.
- Daily inspection of exit site: visually and by palpation.

INJECTION & INJECTION CAPS

- Protocols need to be in place for disinfecting, accessing, changing caps with Chlorhexidine >0,5% solutions.
- Important aspect of care in reducing the risk of catheter related bloodstream infection.
- No specific guidance in terms of how long to disinfect due to lack of clear evidence.
- Change *at least* every 7 days.

DRESSINGS

- Sterile dressings only.
- Change at established intervals:
  - Gauze – every 48 hours.
  - Transparent – at least every 7 days.
- Chlorhexidine Skin Antisepsis.

NOTE: Gauze under transparent is a gauze dressing– still a common misconception.

CATHETER SITE CARE

- Aseptic technique.
- Sterile gloves and mask – central catheters, extended dwell, patient is immunocompromised.
- Includes disinfection, application of new stabilization device, sterile dressing.
- Preferred: combination of alcohol + chlorhexidine (CDC – best evidence) or + povidone iodine.

Occlusion prevention

- Stop & go flush of the CVC with NaCl 0,9% 10 ml before and after each infusion.
- Stop & go flush of the CVC with NaCl 0,9% 20 ml after infusion of blood products, after blood collection.
- Closing only with NaCl 0,9% of short and medium term devices in intra-hospital use.
- Use neutral pressure NFCs.
- Avoid drugs cocktails.
- Use infusion pump for NPT.
- Do not use heparin in the line with lipid emulsions.
- Choose VAD of suitable size and / or power injectable.

Clinical competencies

"The nurse providing infusion therapy shall be proficient in its' clinical aspects, **shall have validated competency..**"

"Development of clinical competencies **should be the responsibility of the nurse** and should be included in the organization's policies and procedures"

Literature reference

- Baskin, J. and Spyridis, G. Management and Complications of Central Venous Catheters Cure4Kids #1516. Released on Cure4Kids: 25 Nov 2008.
- Boxtel AJH, Fliedner MC, Borst DM, Teunissen SCCM. Peripherally inserted central venous catheters: first results after the introduction in a Dutch university medical Center. J Vasc Access. 2008;13(3):128–33.
- Brunelle D. Impact of a dedicated infusion therapy team on the reduction of catheter-related nosocomial infections. J Infus Nurs. 2003;26(6):362–6.
- Cadman A, Lawrance JA, Fitzsimmons L, Spencer- Shaw A, Swindell R. To clot or not to clot? That is the question in central venous catheters. Clin Radiol. 2004;59(4):349–55.
- Carraro F, Cicalese MP, Cesaro S et al (2013), *Guidelines for the use of long-term central venous catheter in children with hemato-oncological disorders. On behalf of supportive therapy working group of Italian association of pediatric hematology and oncology (AIEOP).* Ann Hematol 92:1405–1412
- Carson S M (2004), *Chlorhexidine versus Povidone-iodine for central venous catheter site care in children*, J Ped Nurs, 19: 74-80
- Centers for Disease Control and Prevention. Guidelines for the prevention of intravascular catheter-related infections. MMWR 2002; 51(RR-10): 1-32.
- Cesaro S, Cavaliere M, Pegoraro A et al (2016), *A comprehensive approach to the prevention of central venous catheter complications: results of 10-year prospective surveillance in pediatric hematology-oncology patients*. Ann Hematol 95:817-25
- Cesaro S, Tridello G, Cavaliere M, Magagna L, Gavin P, Cusinato R, Zadra N, Zanon F, Zanesco L, Carli M, (2009) *Prospective, randomized trial of two different modalities of flushing central venous catheters in pediatric patiens with cancer,* J Clin Oncol., 27 (12): 2059-2065
- Chopra V, Anand S, Hickner A, Buist M, Rogers MA, Saint S, Flanders SA. Risk of venous thromboembolism associated with peripherally inserted central catheters: a systematic review and meta-analysis. Lancet. 2013;382:311–25.
- Conway M A, McCollom C, Bannon C (2014), *Central Venous Catheter flushing recommendations: a systematic evidence-based practice review*, Journal of Pediatric Oncology Nursing, 31 (4) 185-190
- Crocoli A, Tornesello A, Pittiruti M et al (2015), *Central venous access devices in pediatric malignancies: a position paper of Italian association of pediatric hematology and oncology.* J Vasc Access 16:130–136
- Debourdeau P, Kassab Chahmi D, Le Gal G, Kriegel I, Desruennes E, Douard MC, Elalamy I, Meyer G, Mismetti P, Pavic M, Scrobohaci ML, L.vesque H, Renaudin JM, Farge D, Working group of the SOR; French National Feberation of Cancer Centers. SOR guidelines for the prevention and treatment of thrombosis associated with central venous catheters in patients with cancer: report from the working group. Ann Oncol. 2009;20(9):1459–71.
- Fallouh N, McGuirk HM, Flanders SA, Chopra V. Peripherally inserted central catheter-associated deep vein thrombosis: a narrative review. Am J Med. 2015;128:722–38.
- Frey, AM, Schears, GJ. Why are we stuck of tape and suture?- A review of catheter securement devices. JIN 2006;29: 34-38.
- Giordano P, Saracco P, Grassi M et al (2015), *Recommendations for the use of long-term central venous catheter (CVC) in children wit hemato-oncological disorders: management of CVC-related occlusion and CVC-related thrombosis. On behalf of the coagulation defects working group and the supportive therapy working group of the Italian Association of Pedriatric Hematology and Oncology (AIEOP)*, Ann Hematol 94:1765-1776
- Goossens GA, J.r.me M, Janssens C, Peetermans WE, Fieuws S, Moons P, Verschakelen J, Peerlinck K, Jacquemin M, Stas M. Comparing normal saline versus diluted heparin to lock non-valved totally implantable venous access devices in cancer patients: a randomised, non-inferiority, open trial. Ann Oncol. 2013;24(7):1892–9.
- Gorski L, Hadaway L, et al. Infusion therapy standards of practice. J Infus Nurs. 2016;39:1S.
- Gorski, LA. Ethical decision making and repair of a patient's catheter. *J Infus Nurs.* 2007;30(4):203-204.
- Ho KM, Litton E. Use of chlorhexidine-impregnated dressing to prevent vascular and epidural catheter colonization and infection: a meta-analysis. *J Antimicrob Chemother*. 2006;58(2):281–287
- IDSA Guidelines: Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update of Infectious Disease Society of America (2009)
- Infusion Nurses Society. Infusion Nursing Standards of Practice. *J Infus Nurs.* 2006;29(1S):S1–S92.
- Maki DG, Kluger DM, Crnich CJ. The risk of bloodstream infection in adults with different intravascular devices: a systematic review of 200 published prospective studies. Mayo Clin Proc. 2006;81:1159–71.
- Moureau N, Lamperti M, Kelly LJ, Dawson R, Elbarbary M, van Boxtel AJH, Pittiruti M. Evidence-based consensus on the insertion of central venous access devices: definition of minimal requirements for training. Br J Anaesth. 2013:1–10.
- Nifong TP, McDevitt TJ. The effect of catheter to vein ratio on blood flow rates in a simulated model of peripherally inserted central catheters. Chest. 2011;140(1):48–53.
- O'Grady NP, Alexander M, Burns LA et al (2011), *Guidelines for the prevention of intravascular catheter-related infections*. Clin Infect Dis 52:162–193Skinner Al, (2008), *Prevention and management of central venous catheter occlusion and thrombosis in children with cancer,* Pediatr. Blood Cancer, 50: 826-830
- Pikwer A, .keson J, Lindgren S. Complications associated with peripheral or central routes for central venous cannulation. Anaesthesia. 2012;67:65–71.
- Rivera AM, Strauss KW, van Zundert A, Mortier E. The history of peripheral intravenous catheters: how little plastic tubes revolutionized medicine. Acta Anaesthesiol Belg. 2005;56(3):271–82.
- Rutledge D, Orr M. Effectiveness of intravenous therapy teams. J Clin Innovat. 2005;8(2):1–24
- Features and selection of vascular access devices. Seminars in Oncology Nursing, Vol. 22, No 2 May, 2010: p 97

Neutropenia & Fever

Early and acute complications in BMT setting, diagnosis and management:

- **Management of mucositis & oral care, nausea, vomiting and pain management**
- **Central venous access devices (care of CVAD: Hickman, port and PICC)**
- **Neutropenic fever, management of thrombocytopenia and bleeding**

Alberto Castagna, Italy

Fever

A single oral temperature measurement of ≥ 38,3°C or a temperature of ≥ 38,0°C sustained over 1h period.

Neutropenia

Increase susceptibility to infection is likely when the neutrophil count falls below 1,0x10e9 with escalating risk at < 0,5x 10°9 and <0,1x10e9.

The risk of infection is greater the faster the rate of decline of the neutrophil count and the longer the duration of neutropenia especially if neutropenia lasts for > 10 days.

Do not delay administration of antibiotics whilst awaiting WCC results.

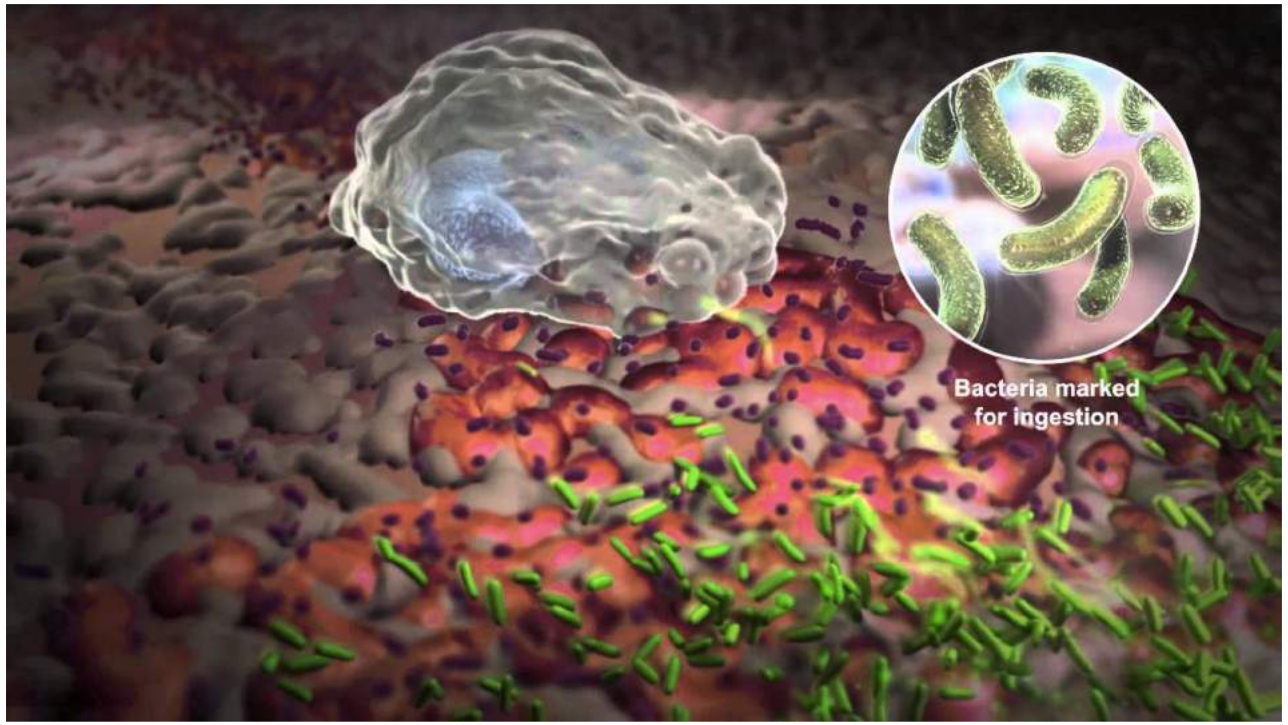
Facts

Neutropenia is the most common dose-limiting toxicity of chemotherapy.

Neutropenia is asymptomatic.

Symptoms are associated with neutropenis complication (e.g. infection, which leads to fever).

Neutrophil



First defensive line against infections.

They digest bacterial organisms and debris.

They increase during infections or acute traumas.

Half-life in a circle of 6 - 8 hours,

Normal values: 40 – 75 % Total Leukocytes
Adults: 1,500 - 7,000 mm3

Background

- **Infections remain a main cause of morbidity and mortality in patients undergoing HSCT**

- The principal risk factors for infection after HSCT:
  - Status of the haematological disease
  - Co-morbidities on the patient
  - The degree of neutropenia
  - The disruption of anatomical barriers (mucocitis, indwelling catheters)
  - T- and B- cell function
  - Immunosuppressive therapy

Febrile Neutropenia

Fever ≥38,3°C or ≥38°C on 2 times and ANC <500/mm^3 or <1000/mm^3 and predicted to fall to <500/mm^3.

Have a cold chill – clinical status.

Fever neutropenia is the life-threatening and requires urgent attention.

About 70-75% of deaths in acute leukaemia.

About 50% of deaths in patients with solid tumours and related to infections secondary to neutropenia.

60% of febrile neutropenic patients prove to have infections.

16-20% patients with neutrophils <100/mm^3 have a bacteraemia

Fever probably a result of bacteraemia

Gram positive cocci or Gram negative bacilli

Fungal infections tend to occur after patients have received broad-spectrum antibiotics and have had prolonged periods of neutropenia but may present a primary infections.

Grading Neutropenia

GRADE 1 SLIGHT
- **LLN < 1500 / > 1000 cell/mmc³**
- No Risk

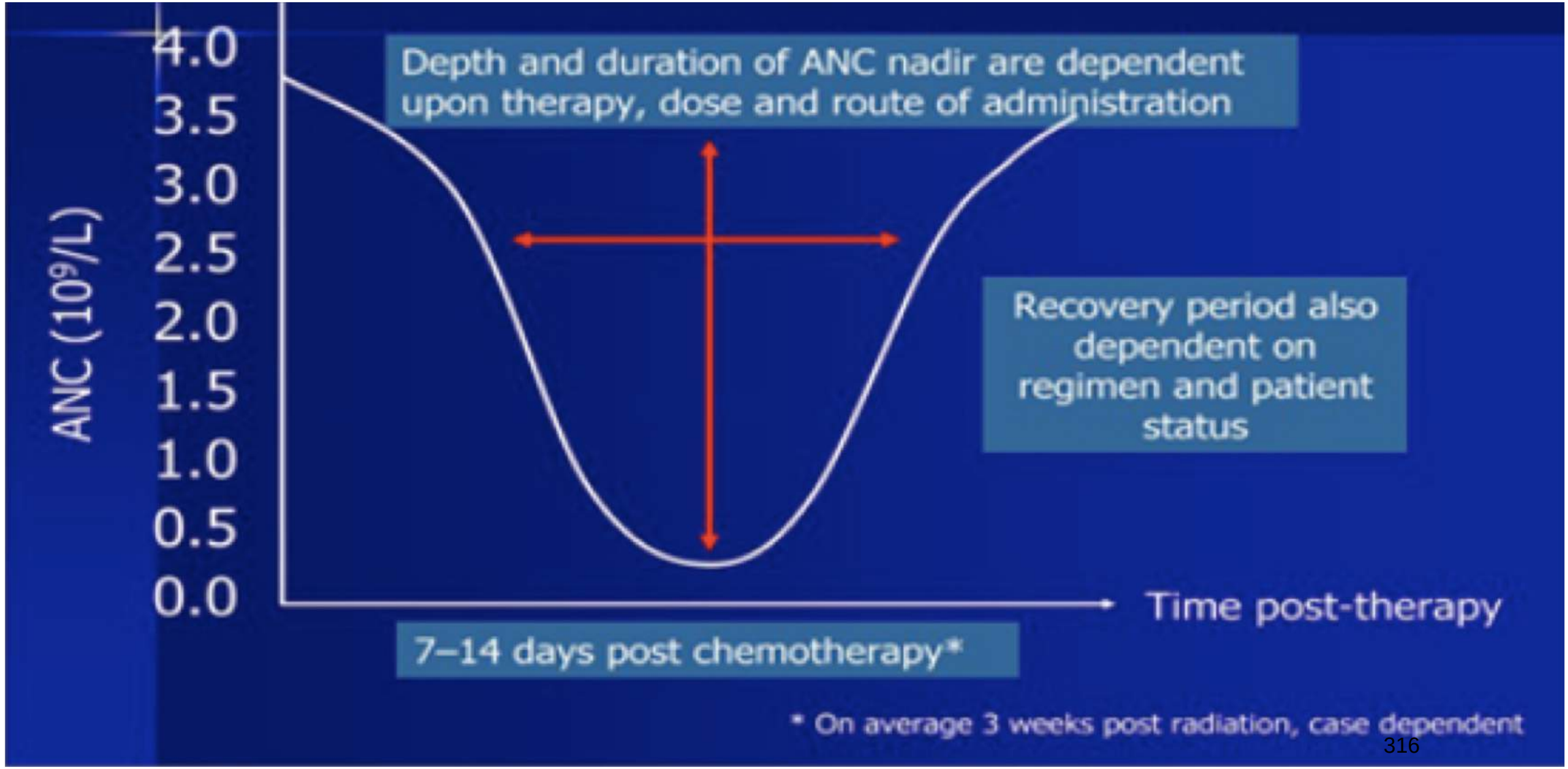
GRADE 2 MODERATE
- **LLN < 1000 / > 500 cell/mmc³**
- Slight increase in risk

GRADE 3 SEVERE
- **LLN < 500/mmc³ ore reduction**
- **LLN < 500/mmc³ in 48h**
- Moderate risk
- Febrile Neutropenia: Present

GRADE 4 DEEP
- **LLN < 500/mmc³ prolonged for more than 7 days**
- **LLN < 100/mmc³**
- High risk
- Febrile Neutropenia: life threatening consequences (e.g. septic shock, hypotension, acidosis, necrosis)

GRADE 5 DEATH
- DEATH

Highest risk of infection is during the nadir period



The sepsis cascade

SIRS

- Systemic Inflammatory Response Syndrome (SIRS) the body's response to a variety of severe clinical insult which may not be infection.

Sepsis

- Systemic inflammatory response to infection.

Severe Sepsis

- Sepsis with acute organ dysfunction or hypoperfusion or hypotensio.

Septic Shock

- A subset of severe sepsis with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include lactic acidosis, oliguria or alteration of mental status.

SIRS – Sepsis or Systemic Inflammatory Response Syndrome

Patients are often described as being “septic” or having “septic shock”

Systemic inflammatory response syndrome (SIRS):

- Temperature >38°C or < 36°C.
- Heath rate > 90/min.
- Respiratory rate > 20/min or $PaCO_2$ < 4,3kPa.
- White cell count > $12x10^9$/L (in those with normal bone marrow activity) <4 $x10^9$/L or >10% bands.

Sepsis is defined as SIRS in response to infection.

Sever sepsis is sepsis associated with:

- Organ dysfunction (altered organ function such that normal physiology cannot be maintained without support).
- Hypotension (systolic blood pressure < 90mmHg or a reduction of > 40mmHg from the patient’s normal in the absence if other causes of hypotension).
- Organ Hypoperfusion (revealed by signs such as lactic acidosis, oliguria, acute alteration of mental status).

Septic shock describes sepsis with hypotension despite adequate fluid resuscitation.

Multiple organ dysfunction syndrome (MODS) describes a state where dysfunction is seen in several organs.

The Patient with Sepsis

Typically, patients with sepsis arrive with the following signs and symptoms:

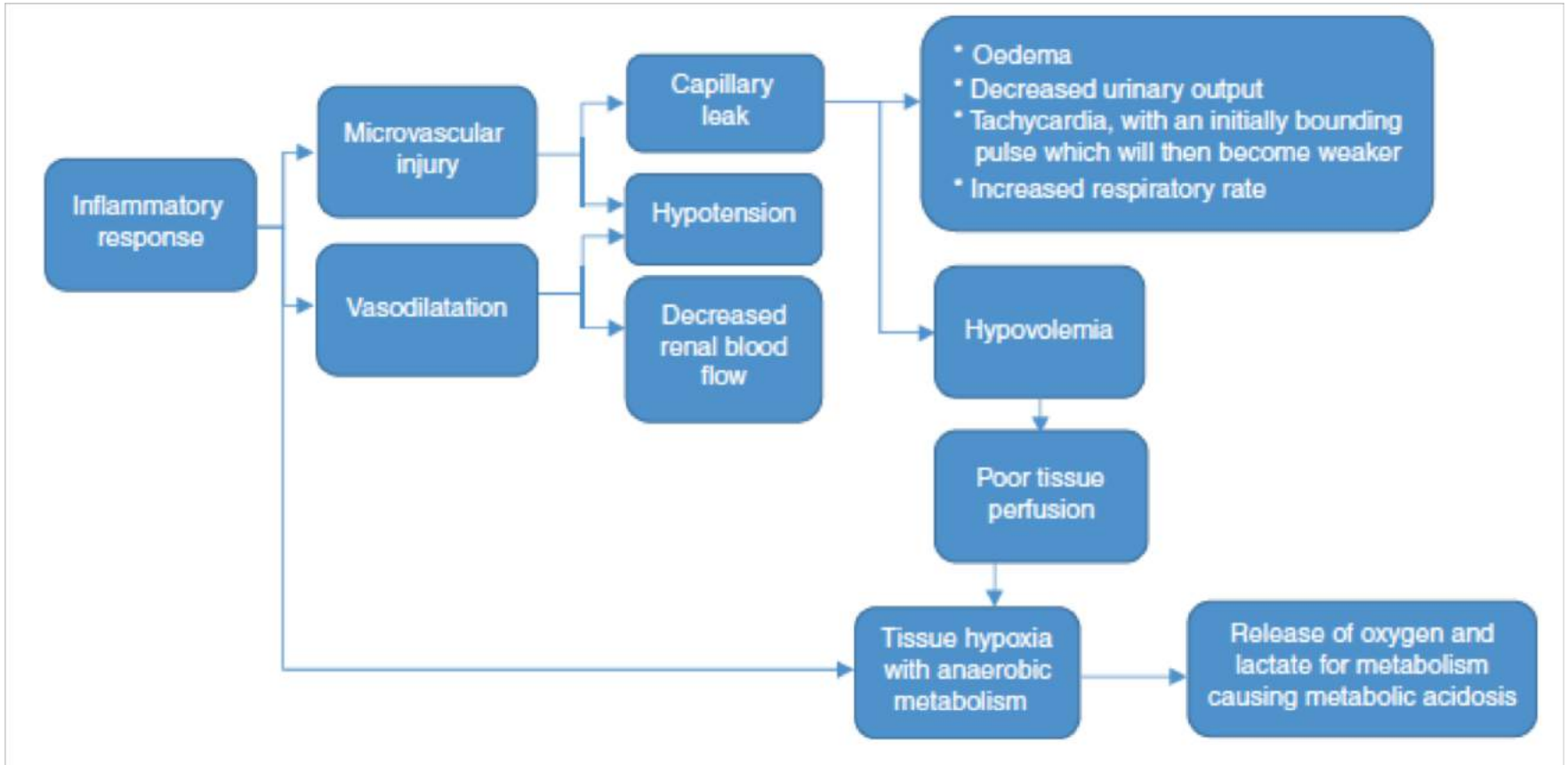
- May or may not be ill appearing.
- Tachycardia.
- Tachypnea.
- Warm, flushed skin.
- Normal blood pressure.
- Normal urine output.
- Bounding pulses.

Remember: Patients presenting with neutropenic sepsis may or may NOT have fever.

Do NOT rely on fever as an indicator of sepsis.

Septic shock

A subset of sepsis with circulatory and cellular/metabolic dysfunction associated with a higher risk of mortality.



The Patient in Septic Shock

The patient in septic shock will typically arrive with the following:

- While typically ill-appearing, these patients may be well appearing upon arrival so do NOT base on looks alone.
- Tachycardia.
- Tachypnea.
- Cool, dry skin.
- Hypotension that is persistent and is not resolved with fluid resuscitation.
- Weak or absent peripheral pulses.
- Decreased Capillary Refill.
- Decreased (or even absolutely NO) urine output.

Sepsis vs Septic shock

Key Similarities

- Tachycardia
- Tachypnea
- Both COULD have Fever
- Both COULD be well-appearing

Key Differences

Pulses

- Sepsis: Bounding
- Progression: Decreased or Absent

Capillary Refill

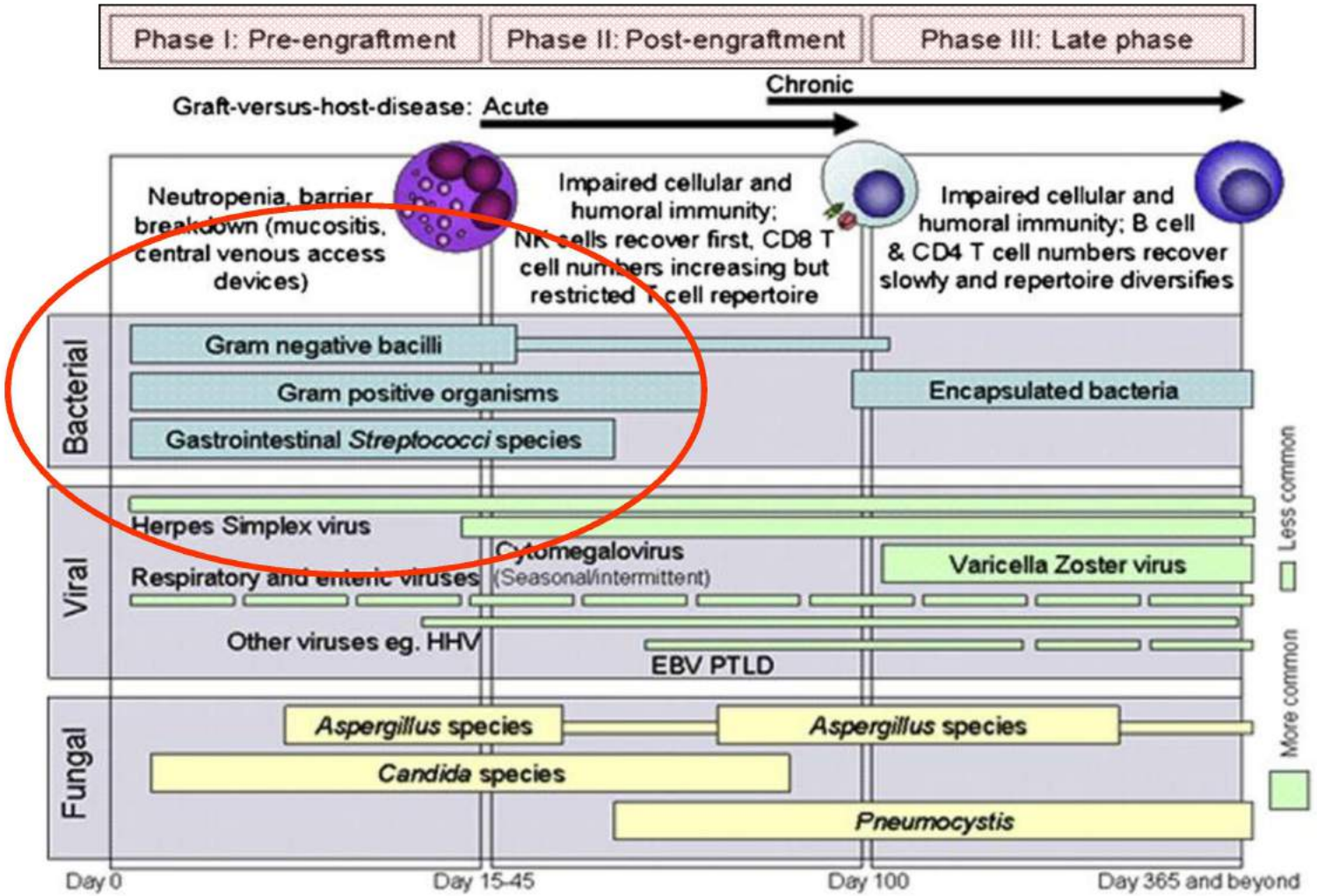
- Sepsis: Normal to Slightly Decreased
- Progression: ≥ 3 seconds

Blood Pressure

- Sepsis: Normal to Slightly Decreased
- Progression: Persistent Hypotension

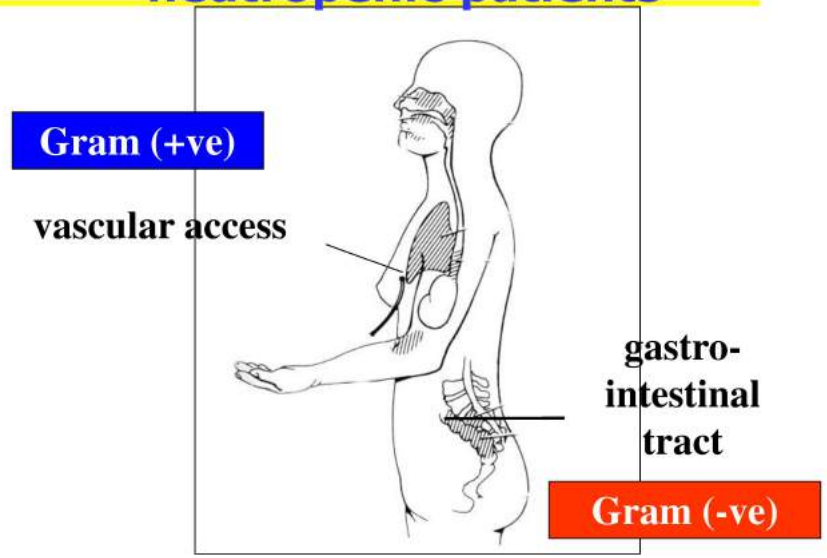
Timeline

Bacteria Infection

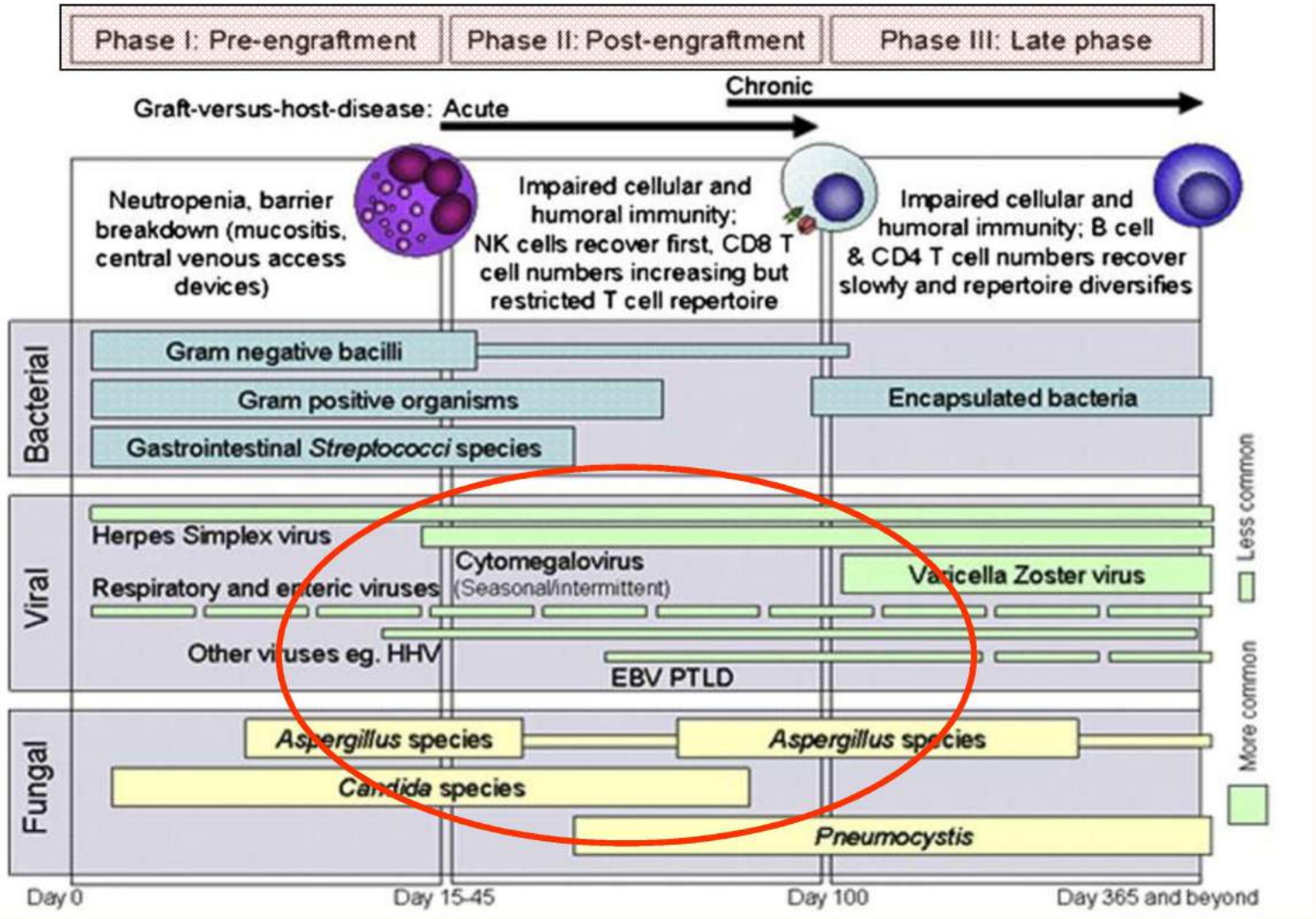


Tomblyn et al. BB&MT 2009

Main sources of infection in neutropenic patients



Timeline



Tomblyn et al. BB&MT 2009

Fungal infections: *Candida*

Relevant species

- *C. albicans* (more common)
- *C. tropicalis*, *C. parapsilosis*
- *C. krusei*, *C. glabrata*

- Entry: GI tract, IV catheter
- Clinical presentation:

Localized: 26-44% oropharingeal, esofagueal

Disseminated: 1-15% (mortality <70%)

Chronic systemic (exceptional)

Virus

- Herpesvirus

  HSV: 70% sero+ pre-SCT.
  Reactivation 2-3rd w (pre-aciclovir 70%)

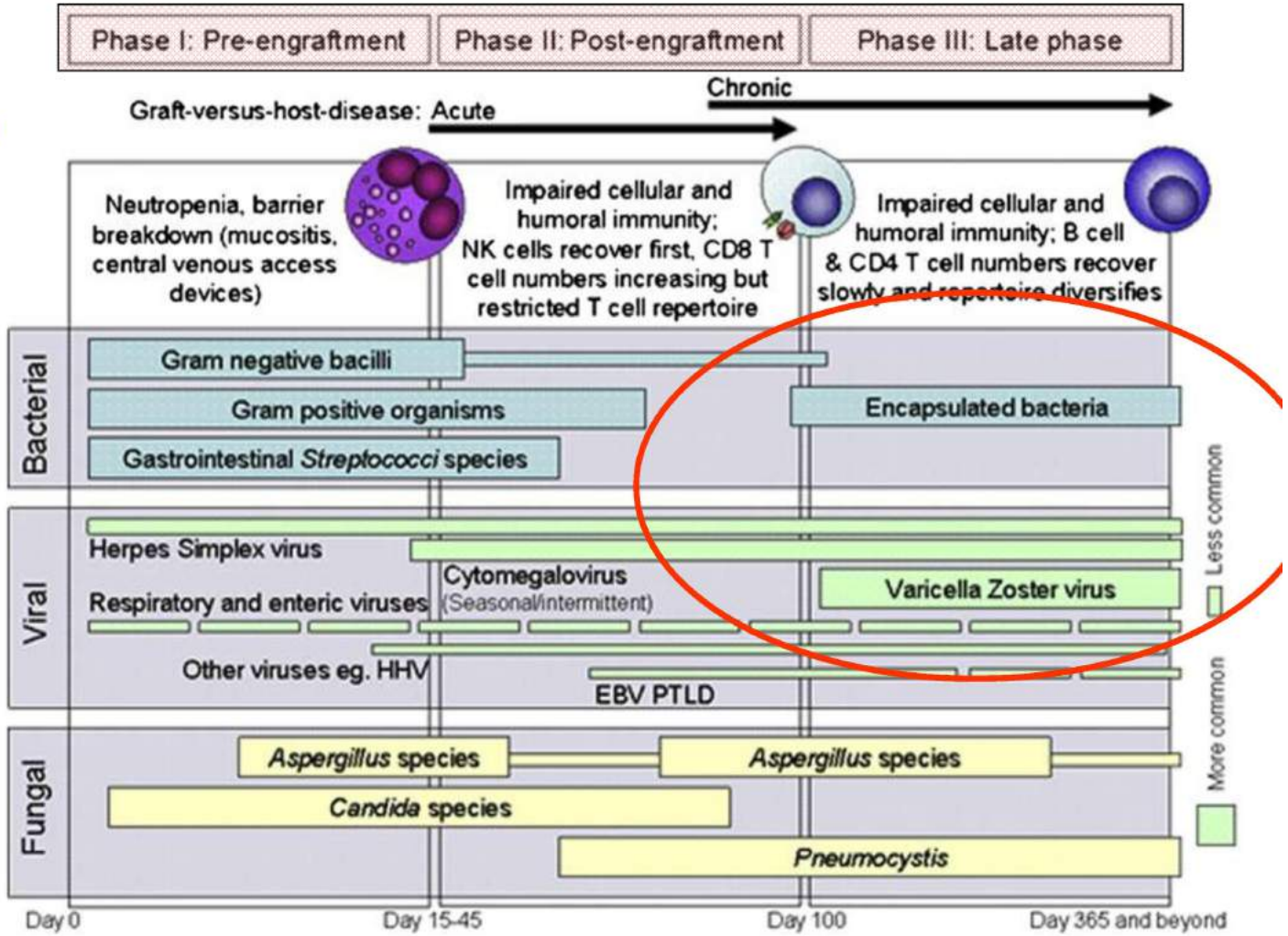
  HHV-6, VEB, CMV
- Enterovirus

  Adenovirus: 5%, 2-3 m SCT;
  disseminated or HC (serotipo 11)

  Coxsackie and rotavirus
- Respiratory

  RSV, parainfluenza, influenza

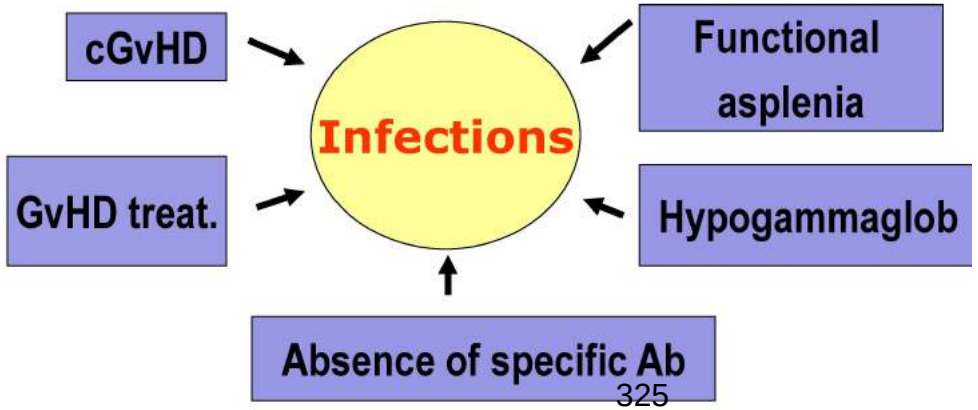
Timeline



Tomblyn et al. BB&MT 2009

Bacterial Infection late after HSCT

Capsulated bacteria
(S. pneumoniae, H. influenzae, N meningitidis)



Patients at high risk for serious complications during fever and neutropenia

Presence of any co-morbid medical problems including but not limited to:

- Hemodynamic instability
- Oral or gastrointestinal mucositis that interferes with swallowing or causes severe diarrhea
- Gastrointestinal symptoms, including abdominal pain, nausea and vomiting, or diarrhea
- Neurologic or mental-status changes of new onset d Intravascular catheter infection, especially catheter tunnel infection d
- New pulmonary infiltrate or hypoxemia, or underlying chronic lung disease

(Friefeld et al 2011)

The patient in septic shock will typically

While typically ill -appearing, these patients may be well appearing upon arrival so do NOT base on looks alone:

- Tachycardia
- Tachypnea
- Cool, dry skin
- Hypotension that is persistent and is not resolved with fluid resuscitation
- Weak or absent peripheral pulses
- Decreased Capillary Refill
- Decreased (or even absolutely NO) urine output

Minimising risk of Neutropenic Complications

- Frequent and correct hand disinfection.
- Good moth care and assessment oral status.
- Protect skin integrity.
- Look out for subtle signs of infection (change in behavior, feeling different without clear explanation).
- Avoid people with infection or recent vaccinated.
- Educate patient and family about signs and symptoms.
- Teach patients the importance of prompt reporting of suspicious changes.

Minimising risk of Neutropenic Complications

In patients with neutropenia effective protocols for hand washing

is the most effective intervention in preventing an infection.

Minimising risk of Neutropenic Complications

High Evidence

- Frequent oral care.
- VAD not placed when neutropenia.
- Antimicrobical prophylaxis if neutropenia.
- <500/mm^3 is expected during > 7 days.
- Construction barriers.
- Prompt action when neutropenic fever.

Minimising risk of Neutropenic Complications

In patients in whom the neutropenia persists for longer than 7 days is

recommended the use prophylactic antibiotics.

How to treat sepsis

1. Early identification of sepsis
2. Immediate antimicrobial therapy
3. Empiric choice of agent
4. Appropriate supportive care

How prompt is prompt in daily practice?

Aim: to assess delay in time to empirical treatment-

Methods:

- Baseline time point registration
  - Moment - fever (38.5°C) signalled
  - Moment – blood cultures taken
  - Moment – physician assesses the patient
  - Moment – first dose of antibiotics is given
- Interventions
- Follow-up time point registration

Nursing care

- Temperature
- Blood pressure
- Pulse
- Respiratory rate
- Oxygen saturation
- AVPU
- Urine output
- Pain

Score Identify the clinical instability level of the patient

Modified Early Warning Score (MEWS)

	4	3	2	1	0	1	2	3	4
Temperature (°C)	<34	34.0-34.5	34.6-35.0	35.1-35.9	DEVIATION FROM NORMAL RANGE	38-38.4	38.5-39.9	40.0-40.4	>40.4
Systolic Blood Pressure (mmHg)	<90	90-99	100-110			150-169	170-189	190-200	>200
Pulse (bpm)	<45	45-49	50-54	55-60		90-99	100-119	120-139	>139
Respiratory Rate (breaths/min)	<8	8-9	10-11			21-25	26-30	31-36	>36
Oxygen Saturations on Oxygen (%)	<88	88-91	92-95	96					
Oxygen Saturations on Air (%)	<85	86-89	90-93	94-96					
AVPU **OR** New CA	**P**ain response		**V**oice response				Confusion **OR** **A**gitation		
Urine Output (mls/hr over 2 hrs)	<10		<20				>250		

Actions from MEWS

Score	Actions
<2	Qualified nurse to review patient at next hand-over
2-3	Qualified nurse to review immediately Repeat observations and instigate therapy as prescribed
4-5	Qualified nurse to review immediately Repeat observations and instigate therapy as prescribed **Junior Doctor to review within 30 minutes**
6-7	Qualified nurse to review immediately Repeat observations and instigate therapy as prescribed **Urgent review by SHO or StR immediately** **PLUS** **Inform Critical Care Outreach Team of patient**
8	Qualified nurse to review immediately Repeat observations and instigate therapy as prescribed **Urgent review by SHO or StR immediately** **PLUS** **Urgent review by Medical Emergency Team (MET) immediately**

AVPU =

A =	Alert
V =	Only responds to Voice
P =	Only responds to Pain
U =	Unresponsive

CA =

C =	Confusion
A =	Agitation

Adapted from: MEWS used at Frimley Park Hospital NHS Foundation Trust

Risk Assessment: Risk Index Score

MASCC - Risk Index Score

BURDEN OF ILLNESS

How sick is the patient at presentation?

5 — 3 — 0

No signs or symptoms | Mild signs or symptoms | Moderate signs or symptoms | Severe signs or symptoms | Moribund

Estimate the burden of illness considering all comorbid conditions

MASCC RISK-INDEX SCORE/MODEL[1]

Characteristic	Weight
• Burden of illness	
► No or mild symptoms	5
► Moderate symptoms	3
• No hypotension	5
• No COPD	4
• Solid tumor or hematologic malignancy with no previous fungal infection	4
• No dehydration	3
• Outpatient status	3
• Age <60 years	2

Score 21 points or higher: lower risk for febrile neutropenia

Maximum of points: 26

Klastersky et al., 2000

Infection risk of cancer patients

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2012
Prevention and Treatment of Cancer-Related Infections

NCCN Guidelines Index
Table of Contents
Discussion

OVERALL INFECTION RISK IN CANCER PATIENTS[a]	DISEASE / THERAPY EXAMPLES	FEVER & NEUTROPENIA RISK CATEGORY (See FEV-2)	ANTIMICROBIAL PROPHYLAXIS[c,d,e,f,g,h]
Low	• Standard chemotherapy regimens for most solid tumors • Anticipated neutropenia less than 7 d	Low	• Bacterial - None • Fungal - None • Viral - None unless prior HSV episode
Intermediate	• Autologous HSCT • Lymphoma • Multiple myeloma • CLL • Purine analog therapy (ie, fludarabine, clofarabine, nelarabine, cladribine) • Anticipated neutropenia 7 to 10 d	Usually HIGH, but some experts suggest modifications depending on patient status. Purine analogs, intermediate risk when used as single agents; when combined with intensive chemotherapy regimens, the risk converts to high.	• Bacterial - Consider fluoroquinolone prophylaxis • Fungal - Consider fluconazole during neutropenia and for anticipated mucositis • Viral - During neutropenia and at least 30 d after HSCT
High[b]	• Allogeneic HSCT including cord blood • Acute leukemia ▸ Induction ▸ Consolidation • Alemtuzumab therapy • GVHD treated with high dose steroids • Anticipated neutropenia greater than 10 d	Usually HIGH, but significant variability exists related to duration of neutropenia, immunosuppressive agents, and status of underlying malignancy	• Bacterial - Consider fluoroquinolone prophylaxis • Fungal - See INF-2 • Viral - during neutropenia and at least 30 d after HSCT

KEY: CLL = chronic lymphocytic leukemia, GVHD = graft versus host disease, HSCT = hematopoietic stem cell transplant, HSV = herpes simplex virus.

HEPA-filtration

- Although well-designed clinical trials have not validated the use of HEPA-filtration, the CDC recommends that allogeneic HSCT recipients be placed in rooms with HEPA-filters (Sullivan et al., 2001; Dadd, McMinn & Monterosso, 2003)
- It is also reasonable to use HEPA filtration in nontransplant patients with prolonged neutropenia. The principal benefit of HEPA filtration ist likely to be related to prevention of mold infections (NCCN, 2012)
- HEPA-filters were protective in highly immunocompromised patients with hematologic malignancies in the setting of an outbreak of aspergillosis (Peters et al., 1998; Russell et al., 2000; Hahn et al., 2002; Dadd et al., 2003)
- TRM was lower and 1-year survival higher for patients with allogeneic SCT treated with HEPA/LAF isolation. This benefit persists after adjusting for other differences in patient-, disease-, and transplant-related variables (Passweg et al., 1998)

Protective Isolation

Results of research: Other measures

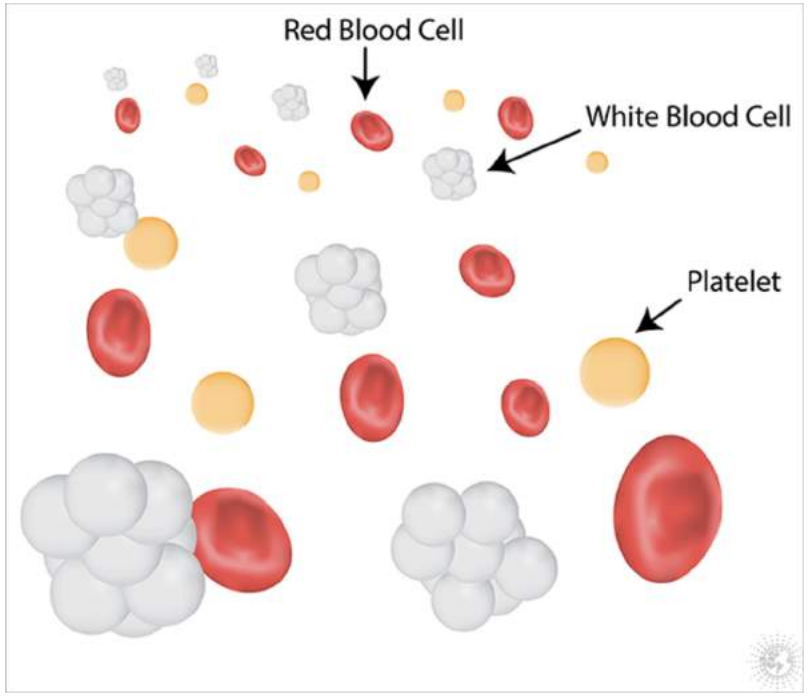
Hand hygiene using soap and water or an antiseptic hand rub	Recommended for practice
Protective gowns if soiling with respiratory secretions is anticipated	Recommended for practice
Routine antifungal prophylaxis for patients with severe, prolonged neutropenia	Recommended for practice
Restrictions for visitors with respiratory symptoms	Recommended for practice
Good mouth care with oral care protocols	Recommended for practice
Colony stimulating factors (CSFs) for all patients with cancer undergoing chemotherapy with >20% risk of febrile neutropenia	Recommended for practice
Keep windows closed	Recommended for practice
No Flowers and plants	Likely to be effective
Annual influenza vaccination	Likely to be effective
Patient education	Likely to be effective
Avoid contact with animal feces, saliva, urine or solid litter box material and all contacts with reptiles	Likely to be effective
Protective Isolation	Effectiveness not established
Diet	Effectiveness not established
Routine use of gowns, gloves and masks	Effectiveness not established
Laminar Air flow	Effectiveness unlikely
Antiseptic bathing	Effectiveness unlikely
Routine antifungal prophylaxis in all patients receiving chemotherapy	Not recommended for practice

Conclusion

- Febrile neutropenia has a significant impact on morbidity and mortality.
- Treating febrile neutropenia is associated with high healthcare costs.
- Management of febrile neutropenia requires:
  - Continuous monitoring;
  - The prompt removal of the source of infection.
- Local and prophylactic antimicrobial strategies will apply.
- Effective hand washing is the most important intervention.

Literature reference

- Clinical Practice Guideline for the Use of Antimicrobial Agents in Neutropenic Patients with Cancer: 2010 Update by the Infectious Diseases Society of America Clinical Practice Guideline Clinical Infectious Diseases 2011;52
- Daniels R, et al. The sepsis six and the severe sepsis resuscitation bundle: a prospective observational cohort study. Emerg Med J. 2011;28:507–12. E-pub 2011, October 29.
- E-learning package Sepsis and Sepsis Six. http://sonet.nottingham.ac.uk/
- Flowers C, Seidenfeld J, Bow EJ, et al. Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol 2013; 31: 794-810
- Gea-Banacloche J Evidence Based approach to treatment of febrile neutropenia in hematologic malignancies. Hematology Am Soc Hematol Educ Program 2013
- Hyman J. Neutropenic patients-Are they receiving their antibioticson time? Nursing Monograph. 2005. 15–18.
- Kee PPL, et al. Diagnostic yield of timing blood culture collection relative to fever. Pediatr Inf Dis J. 2016;35(8):846–50.
- L. R. Baden,W. Bensinger,M. Angarone et al., “Prevention and treatment of cancer-related infections” Journal of the National Comprehensive Cancer Network, vol. 10, no. 11, pp. 1412–1445, 2012
- Nesher L, et al. Utility of routine surveillance blood cultures in asymptomatic allogeneic hematopoietic stem cell transplant recipients with indwelling central venous catheters at a comprehensive cancer center. Am J Infect Control. 2014;42:1084–8.
- Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. Intensive Care Med. 2017;43:304–77.
- Rovira M, et al. Chapter 12: Infections after HSCT. In:EBMT-ESH handbook; 2012. p. 196–215.
- Royal College of Physicians. National Early Warning Score (NEWS) standardising the assessment of acute-illness severity in the NHS. 2012.
- Schorr CA, et al. Severe sepsis and septic shock management and performance improvement. Virulence. 2014;5(1):226–35.
- Singer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA. 2016;315(8):801–10.
- Swedish “Pro Sepsis” Programme Group Sepsis. Care Program Severe Sepsis and Septic Shock – Early identification and initial intervention [F.r Svenska Infektionsl.karf.reningen “Pro Sepsis” Programgrupp Sepsis. V.rdprogram sv.r sepsis och septisk chocktidig identifiering och initial handl.ggning. Reviderat oktober 2015] 2015 edition.



Thrombocytopenia and bleeding

Early and acute complications in BMT setting, diagnosis and management:

- **Management of mucositis & oral care, nausea, vomiting and pain management**
- **Central venous access devices (care of CVAD: Hickman, port and PICC)**
- **Neutropenic fever, management of thrombocytopenia and bleeding**

Alberto Castagna, Italy

Background & Introduction

Defined as condition where the number of circulation platelets is < 150 x 10^9/L.

- Reduced blood coagulation and haemostasis.
- Increases risk of bleeding.

Signs and symptoms of thrombocytopenia

- Bleeding.
- Purpura, ecchymosis (bruising) or hematomas.
- Enlarged and tender liver or spleen.
- Headaches.
- Hypotension or tachycardia (adults).
- Prolonged menstruation or increased levels of bleeding during menses.

General causes of thrombocytopenia in patients with cancer

DISEASE-INDUCED

Bone marrow infiltration.

DIC – Disseminated intravascular coagulation.

Platelet function disorders.

ITP – Immune Thrombocytopenic purpura.

TTP – Thrombocytopenic pupura.

Co-morbidities.

TREATMENT-INDUCED

Myelosuppresive chemotherapy.

Radiotherapy.

Non-cytotoxic drugs.

HIT – Heparin Induced Thrombocytopenia

PTP – Post-Transfusion Purpura

Time course of chemotherapy-induced thrombocytopenia

Dependent on the chemotherapy regimen.

- Biggest decrease in platelet count usually occurs in the first few cycles.
- Cumulative effect can be seen over several courses :

  Platelets counts of $< 50 \times 10^9/L$.

A minority of patients will remain refractory and may never recover their platelet function.

Risk factors

RISK FACTORS FOR THROMBOCYTOPENIA

Reduced platelet or Hb level.
Severe or febrile neutropenia.
Type of chemotherapy.
Surgery.
Age.
Diabetes.
Low Haematocrit.
Elevated alkaline phosphatase.

RISK FACTORS FOR BLEEDING

Cancers requiring “aggressive” multimodality treatment.
Initial platelet count <150x 10^9/L.
Prior radiotherapy.
Hight blood pressure.
Increased Temperature.
Constipation.
Co-morbidities.

Evidenced based practice & Indications

Therapies for thrombocytopenia – Platelet Transfusions

Platelet transfusion are the most widely used treatment for thrombocytopenia.

- Prophylactic transfusion to prevent bleeding:
  - Acute Leukaemia: 10 x 10^9/L.
  - Solid tumours: 10-20 10 x 10^9/L.
  - Surgical or invasive procedures: 40-50 10 x 10^9/L.
- Transfusion to treat haemorrhagic episodes:
  - No optimal standard dose: suggest high dose for therapeutic infusions and lower dose for prophylactic infusions.
- Risk associated with platelet transfusion:
  - Alloimmunization, infection, TRALI, allergic and febrile reactions.

Minimising risk of complications – a collaborative approach

- Teach protective measures.
- Highlight timing of greatest risk.
- Encourage patient and family vigilance.
- Educate how to manage potential bleeding episodes.

Impact of thrombocytopenia

	Patients	Health care system
• Mortality Life threatening risk of bleeding	✓	✓
• Morbidity E.g. infection/immune reaction to transfusions	✓	✓
• Reduced chemotherapy dose Risk of cancer spreading	✓	
• Decreases patients' quality of life E.g. limits physical exercise, intimate contact	✓	
• Financial cost of treatment Hospitalisations and transfusions are expensive	✓	✓

Literature reference

- Cella, David ; Beaumont, Jennifer ; Webster, Kimberly ; Lai, Jin-Shei ; Elting, Linda. Measuring the concerns of cancer patients with low platelet counts: the Functional Assessment of Cancer Therapy–Thrombocytopenia (FACT-Th) questionnaire. Supportive Care in Cancer, 2006, Vol.14(12), pp.1220-1231
- Elting, Ls ; Martin, CG ; Hamblin, L ; Chau, Q. PCN13: cost of thrombocytopenia-related bleeding among patients with cancer. Value in Health, 2001, Vol.4(2), pp.88-89
- Kurzrock R. Thrombopoietic Factors in Chronic Bone Marrow Failure States: The Platelet Problem Revisited. Clin Cancer Res March 2 2005 11 (4) 1361-1367;
- Liou, S. ; Stephens, J. ; Carpiuc, K. ; Feng, W. ; Botteman, M. ; Hay, J. Economic Burden of Haematological Adverse Effects in Cancer Patients Clinical Drug Investigation, 2007, Vol.27(6), pp.381-396
- Shuey K.M. Platelet-associated bleeding disorders Seminars in Oncology Nursing, 1996, Vol.12(1), pp.15-27
- Stanworth, S. J. ; Hyde, C. ; Brunskill, S. ; Murphy, M. F. Platelet transfusion prophylaxis for patients with haematological malignancies: where to now?British Journal of Haematology, December 2005, Vol.131(5), pp.588-595
- Webert, Kathryn ; Cook, Richard J ; Sigouin, Chris S ; Rebulla, Paolo ; Heddle, Nancy M. The risk of bleeding in thrombocytopenic patients with acute myeloid leukemia. Haematologica, November 2006, Vol.91(11), pp.1530-7
- Webert, Kathryn E. ; Arnold, Donald M. ; Lui, Yang ; Carruthers, Julie ; Arnold, Emmy ; Heddle, Nancy M. A new tool to assess bleeding severity in patients with chemotherapy-induced thrombocytopenia (CME).(Report). Transfusion, Nov, 2012, Issue 11, p.(1)

Early and acute complications in BMT setting, diagnosis and management

Eugenia Trigoso, Spain

Nurses No Frontiers - Training course for HSCT nurses – India

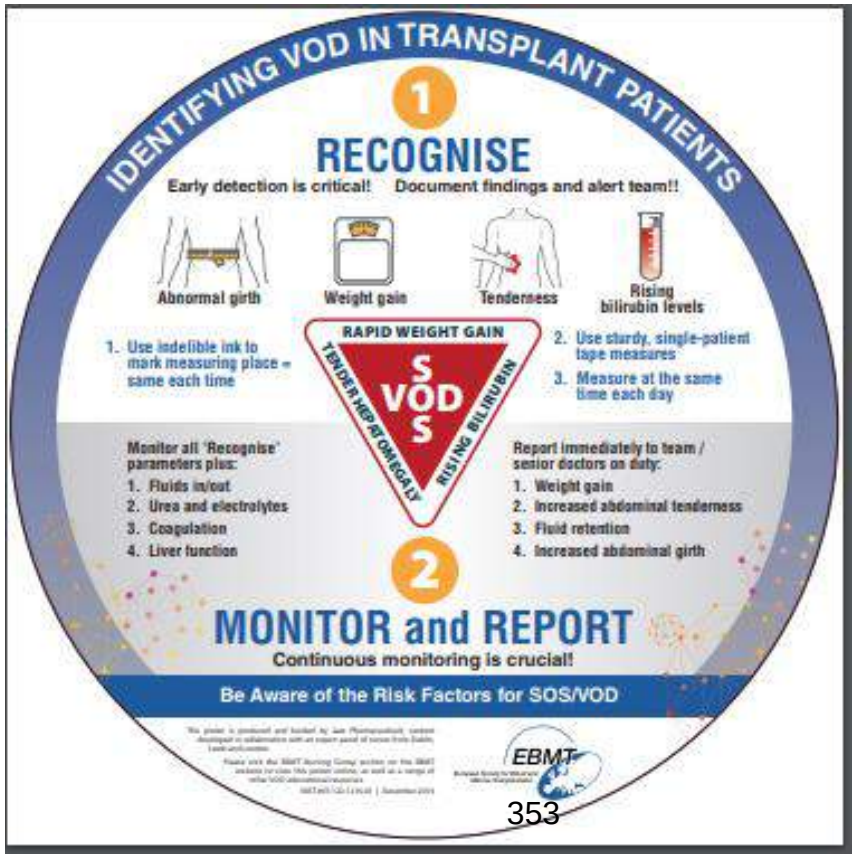
14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

Background & Introduction

- Diagnosis and management of veno-occlusive disease of the liver
- Respiratory infections
- Fungal infections
- Common viral complications

➢CMV

- Multi-resistant bacteria – reducing the spread

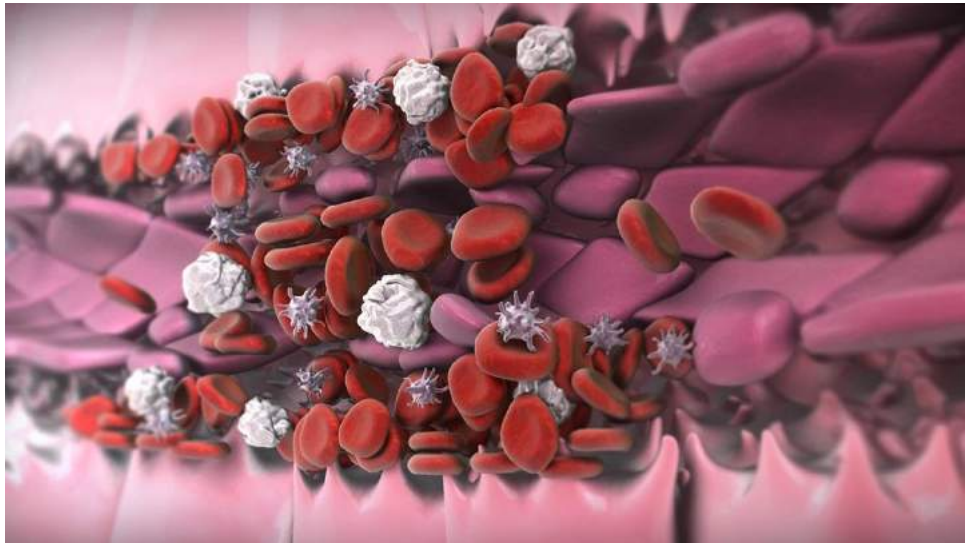


Background & Introduction

- **Diagnosis and management of veno-occlusive disease of the liver**
  - Although it is considered a relatively rare disorder, veno-occlusive disease (VOD) is one of the main causes of overall, non-relapse mortality associated with haematopoietic stem cell transplantation (HSCT)

Management of veno-occlusive disease: the multidisciplinary approach to care. *Wallhult*

  - VOD, also know as sinusoidal obstruction syndrome (SOS), is a potentially life-threatening complication of HSCT
  - Toxicity of HSCT-conditioning regimens causes reduced blood flow in the liver through damage to the sinusoidal endothelial cells
  - VOD occurs in both adults and children:
    - 10–15% of HSCT patients
    - Incidence of up to 60% dependent on risk factors



HSCT, haematopoietic stem cell transplant; VOD, veno-occlusive disease

Background & Introduction

European Journal of Haematology

European Journal of Haematology 98 (322–329)

REVIEW ARTICLE

Management of veno-occlusive disease: the multidisciplinary approach to care

Elisabeth Wallhult[1], Michelle Kenyon[2], Sarah Liptrott[3], Arno Mank[4], Mairéad Ní Chonghaile[5], Aleksandra Babic[6], Jacobine Bijkerk[7], Caroline Bompoint[8], Selim Corbacioglu[9], Roel de Weijer[7], Claudia Fink[10], Sarah Marktel[11], Vivek Soni[12], Sarah Sprenger[13], Eugenia Trigoso Arjona[14], Mohamad Mohty[15]

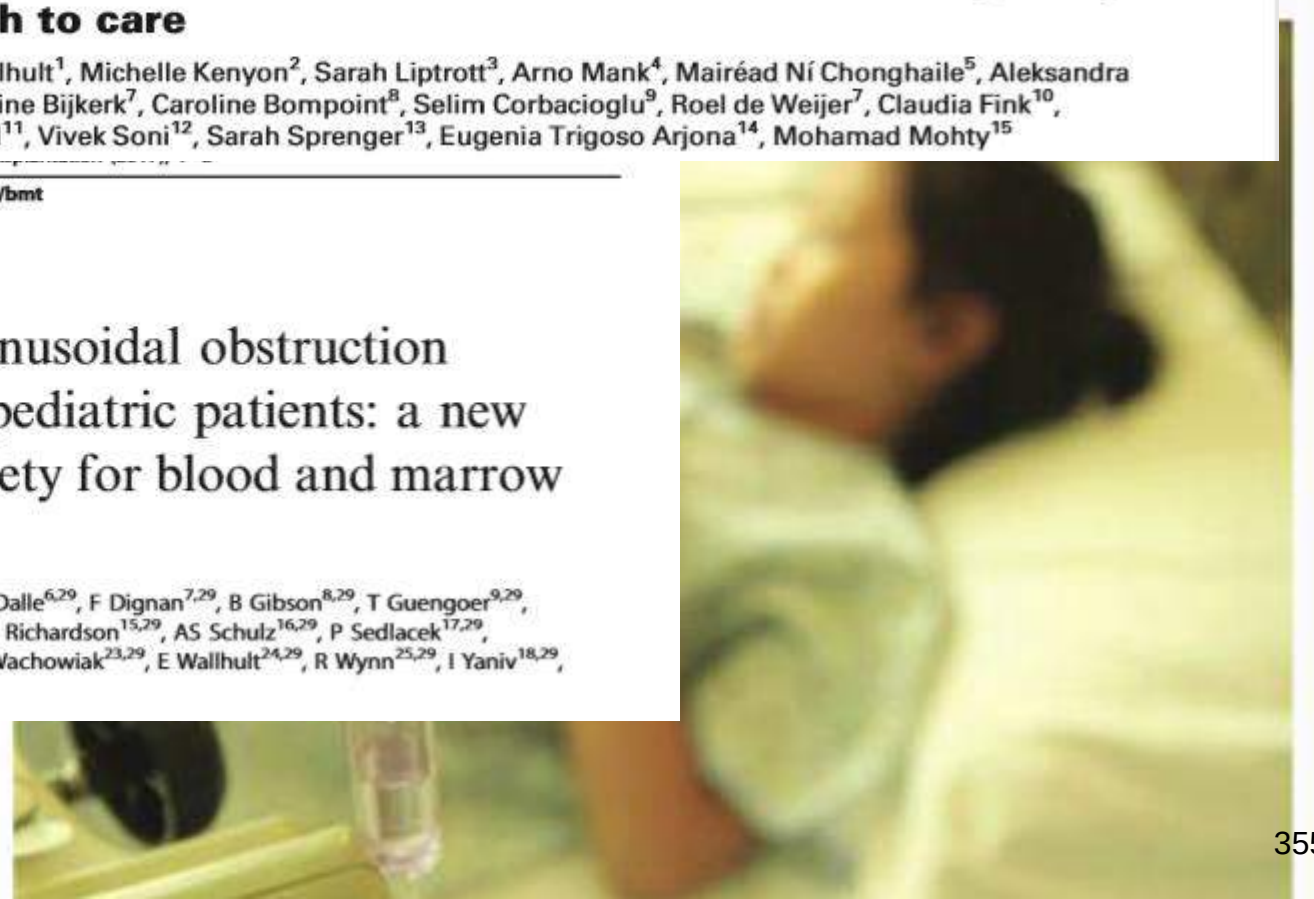
www.nature.com/bmt

OPEN

SPECIAL REPORT

Diagnosis and severity criteria for sinusoidal obstruction syndrome/veno-occlusive disease in pediatric patients: a new classification from the European society for blood and marrow transplantation

S Corbacioglu[1,29], E Carreras[2,29], M Ansari[3,29], A Balduzzi[4,29], S Cesaro[5,29], J-H Dalle[6,29], F Dignan[7,29], B Gibson[8,29], T Guengoer[9,29], B Gruhn[10,29], A Lankester[11,29], F Locatelli[12,29], A Pagliuca[13,29], C Peters[14,29], PG Richardson[15,29], AS Schulz[16,29], P Sedlacek[17,29], J Stein[18,29], K-W Sykora[19,29], J Toporski[20,29], E Trigoso[21,29], K Vetteranta[22,29], J Wachowiak[23,29], E Wallhult[24,29], R Wynn[25,29], I Yaniv[18,29], A Yesilipek[26,29], M Mohty[27,29] and P Bader[28,29]



Background & Introduction

- **Diagnosis and management of veno-occlusive disease of the liver**

Original Seattle criteria[1]

Presentation before Day 30 post-HSCT of two or more of the following:

- Jaundice
- Hepatomegaly and right upper quadrant pain
- Ascites ± unexplained weight gain

Baltimore criteria[2]

Bilirubin ≥2 mg/dL (~34 µmol/L) before Day 21 post-HSCT and at least two of the following:

- Hepatomegaly
- Ascites
- Weight gain ≥5% from baseline

Modified Seattle criteria[3]

Presentation before Day 20 post-HSCT of two of the following:

- Bilirubin >2 mg/dL (~34 µmol/L)
- Hepatomegaly or right upper quadrant pain of liver origin
- Unexplained weight gain of >2% baseline due to fluid accumulation

HSCT, haematopoietic stem cell transplant; VOD, veno-occlusive disease

Background & Introduction

Risk factors for developing VOD in adults

Hepatic-related

- Transaminases >2.5 ULN
- Serum bilirubin >1.5 ULN
- Cirrhosis
- Active viral hepatitis
- Abdominal or hepatic irradiation
- Previous use of gemtuzumab ozogamicin or inotuzumab ozogamicin
- Hepatotoxic drugs
- Iron overload

Transplant-related

- Unrelated donor
- HLA-mismatched donor
- Non T-cell-depleted transplant
- Myeloablative-conditioning regimen
- Oral or high-dose busulfan-based regimen
- High-dose TBI-based regimen
- Second HSCT

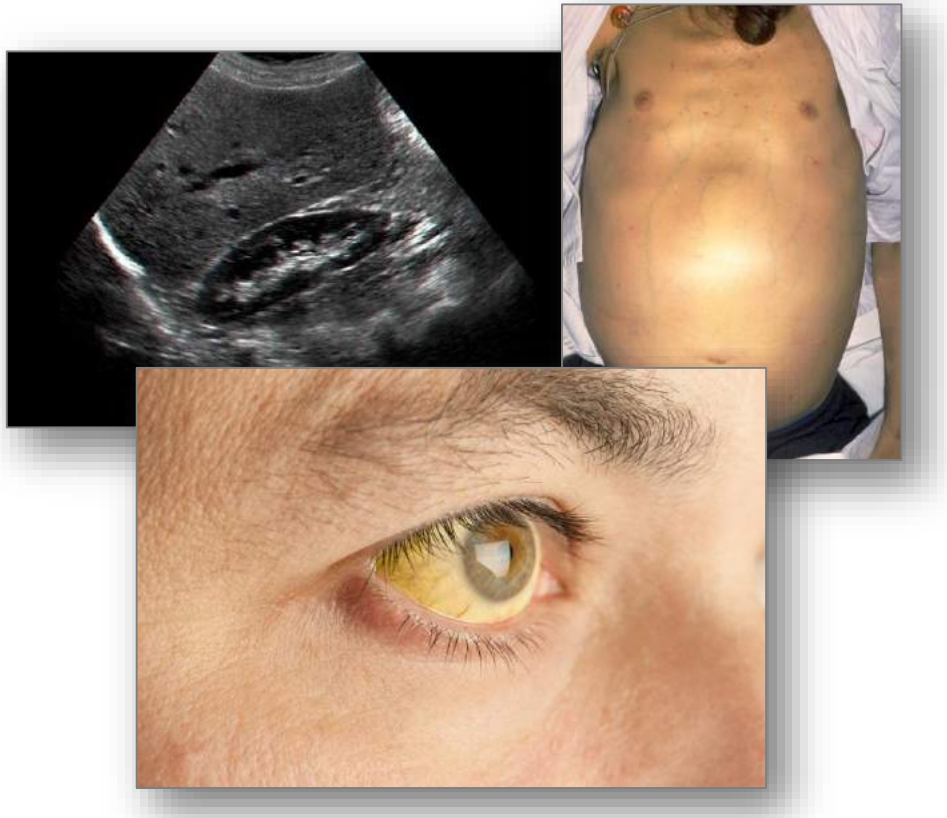
Patient and disease-related

- Older age
- Karnofsky score below 90%
- Metabolic syndrome
- Female receiving norethisterone
- Advanced disease (beyond second CR or relapse/refractory)
- Thalassaemia
- Genetic factors (GSTM1 polymorphism, C282Y allele, *MTHFR* 677CC/1298CC haplotype)

Mohty M et al. *Bone Marrow Transplant* 2016;51:906–12

Background & Introduction

Clinical presentation of VOD in adults



- VOD is characterised by:
  - Rapid weight gain
  - Jaundice
  - Ascites
  - Painful hepatomegaly
  - Right upper quadrant pain
- Symptoms usually present within the first 3–4 weeks following HSCT, but can occur later
- VOD is a progressive disease:
  - Severe VOD is associated with multi-organ failure/multi-organ dysfunction (MOF/MOD) and a high mortality rate (>80%)

HSCT, haematopoietic stem cell transplant;
VOD, veno-occlusive disease

Background & Introduction

Scoring System	
Grayscale ultrasound findings of VOD	**Doppler criteria for diagnosis of VOD**
1. Hepatomegaly	1. Flow demodulation in portal vein
2. Splenomegaly	2. Decrease in spectral density
3. Gallbladder wall thickening greater than 6 mm	3. Reversed portal venous flow or Velocity max less than 10 cm/sec
4. Portal vein diameter greater than 8 mm in children and 12 in adults	4. Portal vein Congestion Index 0.1 or greater
5. Hepatic vein diameter less than 3 mm	5. Hepatic artery resistive index of 0.75 or greater
6. Ascites	6. Monophasic flow in hepatic veins
7. Visualization of para-umbilical vein	7. Flow demonstrated in para-umbilical vein

Background & Introduction

Table 2: New EBMT criteria for severity grading of a suspected SOS/VOD in adults (adapted from ref 12)

	Mild*	Moderate*	Severe	Very severe MOD**
Time since first clinical symptoms of SOS/VOD* **	>7 days	5–7 days	≤ 4 days	Any time
Bilirubin (mg/dl) **Bilirubin (µmol/l)**	≥2 and < 3 ≥34 and <51	≥ 3 and < 5 ≥ 51 and < 85	≥ 5 and < 8 ≥85 and <136	≥8 ≥136
Bilirubin kinetics			Doubling within 48 hours	
Transaminases	≤2 × normal	>2 and ≤ 5 × normal	>5 and ≤ 8 × normal	>8 × normal
Weight increase	< 5%	≥5 % and <10%	≥5 % and <10%	≥10 %
Renal function	<1.2 × baseline at transplant	≥1.2 and < 1.5 × baseline at transplant	≥1.5 and < 2 × baseline at transplant	≥2 × baseline at transplant or others signs of MOD

http://www.hospitalpharmacyeurope.com/handbooks

Background & Introduction

Table 2

EBMT diagnostic criteria for hepatic SOS/VOD in children

- No limitation for time of onset of SOS/VOD

The presence of two or more of the following[a]

- Unexplained consumptive and transfusion-refractory thrombocytopenia[b]
- Otherwise unexplained weight gain on three consecutive days despite the use of diuretics or a weight gain >5% above baseline value
- [c]Hepatomegaly (best if confirmed by imaging) above baseline value
- [c]Ascites (best if confirmed by imaging) above baseline value
- Rising bilirubin from a baseline value on 3 consecutive days or bilirubin ⩾2 mg/dL within 72 h

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5803572/

Background & Introduction

Major differences in hepatic SOS/VOD between adults and children

Criteria	*Children*	*Adults*
Incidence	• Approximately 20% • Up to 60% in high-risk patients	• Approximately 10%
Risk factors	Additional pediatric risk factors: • Infants • Pediatric/genetic diseases with incidences above average	• Established risk factors
Clinical presentation	• Late-onset SOS/VOD in 20% • Anicteric SOS/VOD in 30% • Hyperbilirubinemia, if present: ○ Is frequently pre-existent ○ Occurs late during SOS/VOD ○ Is typical of severe SOS/VOD	• Late-onset SOS/VOD is rare • Anicteric SOS/VOD is rare
Need for proper assessment of ascites and hepatomegaly	• High incidence of disease-related hepatomegaly and ascites pre-HCT	
Treatment	• DF for severe SOS/VOD with MOD/MOF was associated with better results in children compared with adults	
Prevention	• DF demonstrated efficacy for prevention of SOS/VOD in children in a randomized prospective trial	

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5803572/

Background & Introduction

Table 1: New EBMT criteria and modified Seattle criteria for SOS/VOD diagnosis (adapted from refs 12 and 15)

New EBMT criteria *Adult patients*		**Modified Seattle criteria** *Mostly used in paediatric patients*
Classical SOS/VOD *In the first 21 days after HSCT*	**Late-onset SOS/VOD** *>21 days after HSCT*	**Before day 20 post-HSCT**
Bilirubin ≥2mg/dl and two of the following criteria must be present: Painful hepatomegaly Weight gain >5% Ascites	Classical VOD/SOS beyond day 21 OR Histologically proven SOS/VOD OR Two or more of the following criteria must be present: Bilirubin ≥2mg/dl (or 34µmol/l) Painful hepatomegaly Weight gain >5% Ascites AND haemodynamic or/and ultrasound evidence of SOS/VOD	Two of the following criteria must be present: Bilirubin ≥2mg/dl (or 34.2µmol/l) Hepatomegaly or right upper quadrant pain Weight gain (>2% basal weight)
These symptoms/signs should not be attributable to other causes		

http://www.hospitalpharmacyeurope.com/handbooks

Evidenced based practice & Indications

- **Diagnosis and management of veno-occlusive disease of the liver**

Diagnose VOD as soon as possible and begin the treatment without delay

Supportive care still remain usefull

With the availability of defibrotide, the only labeled drug in this disease, there is no reason for using other unlabeled drug for actively treated VOD.

Evidenced based practice & Indications

- **Prophylactic defibrotide** could be considered for patients with HR of VOD, for example:
  - Osteopetrosis
  - HLH
  - JMML
  - 2nd HSCT if MAC for the first
  - Patient younger than 9-12 months with alkylating based MAC
  - Gentuzumab-ozogamycin or Inotuzumab
  - Haplo-T-repleted with 2 alkylating agents followed by PTCY
  - Patients with pre-existing severe liver disease

  - In case of iron overload, try to postpone HSCT and perform active iron chelation

Evidenced based practice & Indications

- **Supportive care-1**

❑Strict fluid balance:

  - Restrict hydration
  - Restrict salt intake
  - Be carefull to use excessive diuretics to prevent intravascular contraction

❑Maintain adequate caloric balance if possible (use gastric feedding rather than parenteral nutrition) ➔ see chapter dedicated to

❑Try to avoid hepatotoxic drugs, including IV lipid formulation

❑Monitor umbilical circumference and body weight (daily, sometime twice daily?) and ultra-sound (weekly?)

•

Helmy A et al. *Aliment Pharmacol Ther* 2006;23:11–25;
Eisenberg S. *Oncol Nurs Forum* 2008;35:385–97; personal communication, J Cooper

Evidenced based practice & Indications

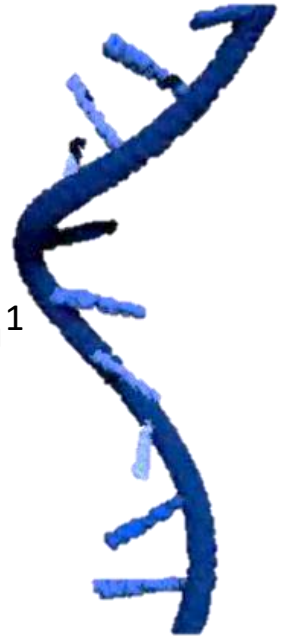
- **Supportive care-2**
- Administer analgesia
- Position patient comfortably – patients can be encouraged to sit up to reduce pressure of the enlarged liver on other organs and to aid breathing
- Administer blood products – due to a derangement of clotting during VOD; volume-reduced platelets can be used in order not to disrupt fluid balance
- Administer electrolytes – when total parenteral nutrition is not viable due to liver damage
- Provide psychological support – as increased bilirubin can cause itchiness, irritability and jaundice

Helmy A et al. *Aliment Pharmacol Ther* 2006;23:11–25;
Eisenberg S. *Oncol Nurs Forum* 2008;35:385–97; personal communication, J Cooper

Evidenced based practice & Indications

- **Curative treatment**
- Defibrotide:
  - 6.25mg/kg x 4/day
  - At least 21 days (Richardson's recommendation)
    - Monitor platelet refractoryness
    - Body-weight stabilization
  - Could be longer depending on symptoms:
  - Be aware of possible rebund after drug taper
  - Higher doses have been administered with success w/o higher toxicity

Evidenced based practice & Indications



- **Curative treatment**
- Defibrotide is a mixture of oligonucleotides derived from porcine intestinal mucosa[1]
- It possesses antithrombotic, profibrinolytic and anti-inflammatory properties that exert a protective effect on the endothelium
- Defibrotide is approved in the EU for the treatment of severe hepatic VOD in patients undergoing HSCT, but is not licensed for prophylaxis[2]
  - It is indicated in adults and in adolescents, children and infants over 1 month[2]
- Defibrotide is recommended by the EBMT and BCSH/BSBMT for the treatment of VOD in adults and children[3,4]
  - The BCSH/BSBMT also recommend defibrotide for the prophylaxis of VOD[4]

EBMT, European Society for Blood and Marrow Transplantation; EU, European Union; HSCT, haematopoietic stem cell transplant; VOD, veno-occlusive disease

Evidenced based practice & Indications

- **Defibrotide administration**

- The recommended dose is 6.25 mg/kg body weight every 6 hours (25 mg/kg/day)
- Administered by intravenous infusion, over 2 hours
- Defibrotide should be diluted prior to use
  - With 5% glucose or 0.9% sodium chloride solution
  - Total volume for infusion based on patient's weight
  - Final concentration for infusion 4–20 mg/mL
- There are limited efficacy and safety data on doses above this level and consequently it is not recommended to increase the dose above 25 mg/kg/day
- Defibrotide should be administered for a minimum of 21 days and continued until the signs and symptoms of severe VOD resolve

EBMT, European Society for Blood and Marrow Transplantation; EU, European Union; HSCT, haematopoietic stem cell transplant; VOD, veno-occlusive disease

Evidenced based practice & Indications

Recommendations for the prevention of VOD in HSCT recipients

- Avoid the use of hepatotoxins (eg, azoles, acetaminophen)
- Identify drug–drug interactions in preparative regimens and modify as appropriate
- Risk-adjust preparative regimen intensity according to haematopoietic cell transplantation-comorbidity index
- Pharmacological monitoring of busulfan (mainly in paediatric patients) and usually only necessary if oral busulfan and not iv busulfan is used
- Avoid the use of progesterone (norethisterone) and oestrogen if possible

Dalle JH, Giralt SA. *Biol Blood Marrow Transplant* 2016;22:400–9

Conclusion

Table 2 Baseline assessments and actions recommended in cases of suspected and confirmed cases of VOD

Baseline	Suspected VOD intensification of monitoring	VOD diagnosed; monitoring in addition to actions for suspected VOD
• Vital signs: temperature, pulse, respiration rate, BP • Baseline weight • Skin: lesions, bleeding, discoloration • Sclera: haemorrhages, jaundice • Abdomen (manual assessment for ascites, e.g. palpation, percussion): abdominal girth[1], bulkiness, the presence of collateral circulation and/or spiders, tractability • RUQ pain: tractability, tenderness, percussion (dullness) • Liver: margins, size, texture • Platelet refractoriness	• At least two times/d: state of consciousness; weight, abdominal girth[1]; physical examination: skin, sclera, abdomen, RUQ pain • At least four times/d: water fluid balance, diuresis, SaO_2 • At least four times/d: vital signs • Two times/d: CBC for PLT refractoriness • Provide appropriate reassurance and psychological support to patient and caregivers • Daily: PT, PTT • Ensure adequate vascular accesses	• Continuous monitoring: vital signs; ventilatory support, if necessary (O_2); fluid restriction; ensure adequate vascular accesses • Careful monitoring: diuresis: bladder catheter, urometer, performance status • Monitoring MOF: cardiac, respiratory and renal function • Psychological support, arrange for transfer to intensive care

Wallhult et al.

EBMT, European Society for Blood and Marrow Transplantation, VOD, veno-occlusive disease

Evidenced based practice & Indications

WARNING!

The following cytotoxic drugs have a clear association with VOD:

- 6-mercaptopurine
- 6-thioguanine
- Actinomycin D
- Azathioprine
- Busulfan*
- Cytosine arabinoside

- Cyclophosphamide*
- Dacarbazine
- Gemtuzumab ozogamicin
- Inotuzumab ozogamicin
- Melphalan*
- Oxaliplatin
- Urethane

Conclusion

Summary of VOD diagnosis

- VOD is characterised by rapid weight gain, ascites, painful hepatomegaly, jaundice
- The Bal diagnose VOD cli
- The nev ude diagnos a for severity grading
- A differ ions that share V
- Risk fact plant-related

"The careful monitoring of HSCT patients allows early detection of the symptoms associated with VOD and timely treatment, ultimately improving patient outcomes.

As part of a multidisciplinary team, nurses have an essential role to play, from pretransplant assessment to medical management and overall care of the patient.

Physicians and pharmacists have a responsibility to facilitate education and training so that nurses can work effectively within that team."

EBMT, European Society for Blood and Marrow Transplantation, VOD, veno-occlusive disease

Literature reference

1.-Wallhult E., Quinn B. (2018) Early and Acute Complications and the Principles of HSCT Nursing Care. In: Kenyon M., Babic A. (eds) The European Blood and Marrow Transplantation Textbook for Nurses. Springer, Cham

2.-http://www.hospitalpharmacyeurope.com/haematology/treating-hepatic-veno-occlusive-disease

3.-Diagnosis and **severity criteria** for **sinusoidal obstruction** syndrome/veno-occlusive disease in pediatric patients: a new classification from the European society for blood and marrow transplantation.
Corbacioglu S, Bone Marrow Transplant. 2018 Feb;53(2):138-145. doi: 10.1038/bmt.2017.161. Epub 2017 Jul 31.

4.- Revised **diagnosis** and **severity criteria** for **sinusoidal obstruction** syndrome/veno-occlusive disease in adult patients: a new classification from the European Society for Blood and Marrow Transplantation.
Mohty M, et al.Bone Marrow Transplant. 2016 Jul;51(7):906-12. doi: 10.1038/bmt.2016.130. Epub 2016 May 16.

5.-Hepatic Veno-Occlusive Disease after Hematopoietic Stem Cell Transplantation: Risk Factors and Stratification, Prophylaxis, and Treatment.
Dalle JH, Giralt SA. Biol Blood Marrow Transplant. 2016 Mar;22(3):400-9. doi: 10.1016/j.bbmt.2015.09.024. Epub 2015 Oct 23. Review.

6.-Consensus Report by Pediatric Acute Lung Injury and Sepsis Investigators and Pediatric Blood and Marrow Transplantation Consortium Joint Working Committees: Supportive Care Guidelines for Management of Veno-Occlusive Disease in Children and Adolescents, Part 1: Focus on Investigations, Prophylaxis, and Specific Treatment, Rajinder P.S. Et col. Biology of Blood and Marrow Transplantation, Volume 23, Issue 11, 2017. Pages 1817-1825, ISSN 1083-8791,

Respiratory infections

Background & Introduction

- Respiratory infections

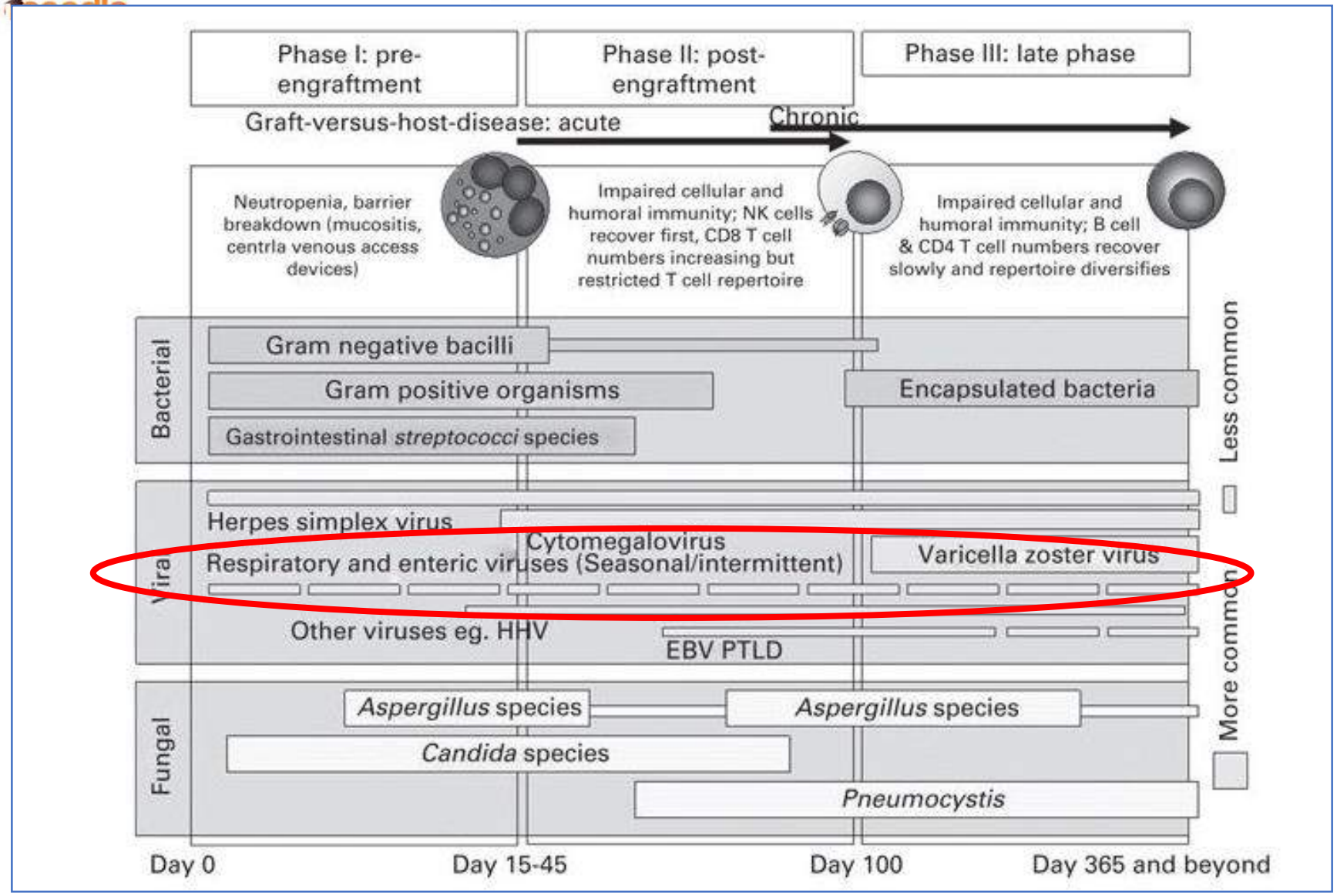
❖ **Pulmonary infections** are the most common complication and a primary cause of death in patients with a malignancy.

- Produce a wide variety of symptoms, signs, and radiographic appearances.
- Tend to occur after chemotherapy or during the neutropenic phase soon after HSCT.

❖ Clinical management of such infection is complex because any microorganism can affect the patient at any time in the course of the hematologic disease, depending mainly on the net state of immunosuppression.

Adapted from Feigin and Cherry's Textbook of Pediatric Infectious Diseases: 7th Edition

Background & Introduction



Phases of opportunistic infections among allogeneic HCT recipients. HHV6, human herpesvirus 6; NK, natural killer; PTLD, post transplant lymphoproliferative disease.

Bone Marrow Transplantation (2009) 44, 457–462

Background & Introduction

Factors affecting the risk of infections

Factor	*Risk of infection*
Type of transplant	Higher risk with allogeneic, lower risk with autologous or syngeneic, depending on graft manipulation and clinical setting, including previous therapies
Time from transplant	Lower risk with more time elapsed from transplant
Pre-transplant factors	Higher risk with extensive pre-transplant immunosuppressive therapy (for example, fludarabine, clofarabine), prolonged pre-transplant neutropenia or pre-transplant infection
GVHD	Higher risk with grade III–IV acute GVHD or extensive chronic GVHD
HLA match	Higher risk with HLA-mismatched donors, particularly with haploidentical donors
Disease (for example, leukemia) status	Higher risk with more advanced disease at the time of transplant
Donor type	Higher risk with marrow-unrelated donor than with a fully matching sibling donor
Graft type	Highest risk with cord blood, intermediate risk with BM and lowest risk with CSF-mobilized blood stem cells. Higher risk with T-cell-depleted grafts (depending on method used)
Immunosuppression after transplant	Higher with immunosuppressive drugs, in particular with corticosteroids, anti-thymocyte globulin and alemtuzumab
Conditioning intensity	Lower risk in the first 1–3 months post transplant with low-dose chemo/radiotherapy
Neutrophil engraftment	Higher risk with delayed engraftment/non-engraftment

Bone Marrow Transplantation (2009) 44, 457–462

Background & Introduction

- Respiratory infections

Figure 10-2. Oncology Medications Potentially Toxic to the Lungs

- All-trans-retinoic acid (ATRA)
- Amphotericin B
- Antithymocyte globulin
- Arsenic trioxide
- Bis-chloroethyl nitrosourea (carmustine or BCNU)
- Bleomycin
- Busulfan
- Chlorambucil
- Colony-stimulating factors (such as granulocyte–colony-stimulating factor)
- Corticosteroids
- Cyclophosphamide
- Cytosine-arabinoside (high-dose cytarabine or ARA-C)
- Deferoxamine
- Etoposide
- Fludarabine
- Gemcitabine
- Hydroxyurea
- Imatinib
- Interferons (IFN α and β)
- Liposomal amphotericin B
- Melphalan
- Methotrexate
- Procarbazine
- Rituximab
- Thalidomide
- Vinca alkaloids (such as vincristine)

HEMATOPOIETIC STEM CELL TRANSPLANTATION: A MANUAL FOR NURSING PRACTICE, SECOND EDITION

Background & Introduction

- Respiratory infections

The principal cause of infection is:

- the severe immunocompromised status of the patients from the disease process (malignant or nonmalignant),
- conditioning regimens (nonmyeloablative and myeloablative),
- and immunosuppressive prophylaxis to prevent and treat GVHD.

The most common in post-transplant recipients (Escuissato et al. (2005)

- viral infections (51%)
- bacterial infections (23%),
- fungal infection (19%),
- and protozoal infections (less than 1%).

- In 5% of the cases examined, patients had two or more infectious agents concurrently.
- These infections occurred despite prophylaxis with antibiotics and antivirals, particularly during the initial neutropenic period.
- Nonmyeloablative conditioning regimens before transplantation can reduce the risk of pulmonary infection by more than half. (Meijer et al. (2004)

Background & Introduction

Respiratory infections

Sources of infection:

- ❑ central venous catheters,
- ❑ innate flora of the mouth, gut, and skin,
- ❑ dormant infections,
- ❑ and infections occurring in the hospital environment with interaction between the patient and staff, family, and friends.

Additional research has exposed **stem cell units themselves as being a source of potential infection**
Cases of contaminated stem cell units are rare but **do require ongoing monitoring for quality, both in the laboratory and at the bedside** (McCann et al., 2004).

Background & Introduction

Table 2: Infectious Acute Pulmonary Complications in Patients with Hematologic Malignancy

Pulmonary Complication	Clinical Setting	Radiologic Findings	Next Step in Diagnostic Evaluation
Bacterial pneumonia	Neutropenia, severe immunocompromise	Segmental or lobar consolidation*	Blood culture, sputum study, analysis of BAL fluid
Fungal pneumonia (eg, aspergillosis)	Neutropenia after chemotherapy, neutropenia at <30 days after HSCT	Angioinvasive aspergillosis: "halo" sign, segmental or subsegmental pleura-based consolidation, cavitation during convalescence Airway-invasive aspergillosis: centrilobular nodules, peribronchial or peribronchiolar consolidations	*Aspergillus* galactomannan antigen test, detection of *Aspergillus* in BAL fluid or lung tissue samples
Pneumocystis jiroveci–induced pneumonia	Impaired cellular immunity at 30–100 days after HSCT	Widespread perihilar ground-glass opacities	Detection of *P jiroveci* in BAL fluid
CMV-induced pneumonia	Impaired cellular immunity at 30–100 days after HSCT	Ground-glass opacities, micronodules, airspace consolidation	Detection of CMV in BAL fluid or lung tissue samples

Note.—CMV = cytomegalovirus.
*The use of CT is helpful for early detection of pneumonia in symptomatic patients without plain radiographic abnormalities.

Background & Introduction

- Respiratory infections

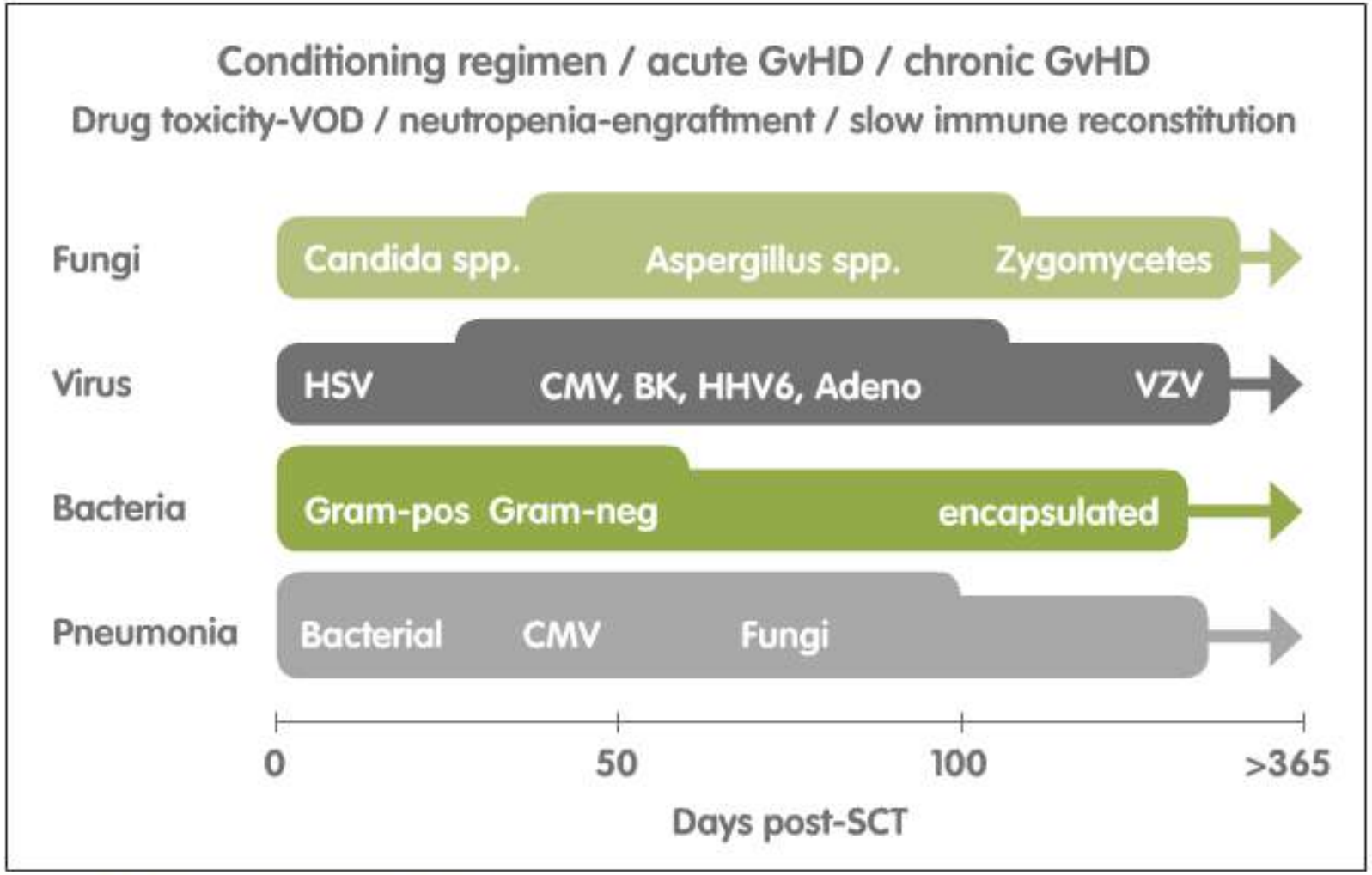


Figure 1. Infectious complications after HSCT

Background & Introduction

- Respiratory infections
- **Pneumonia. Diagnostic approach**
  - To determine the cause of pneumonia**, blood cultures** are performed routinely; however, **the results may be of limited value**.
  - Similarly, **sputum** analysis is often low yield, and the results **are difficult to interpret**.
  - The standard test for diagnosing the cause of a pulmonary infection is therefore microscopic examination of BAL fluid sampled with bronchoscopy.
  - However, this test is invasive, although relatively safe, and it can lead to a rapid diagnosis.
  - Exposure, clinical presentation and imaging may trigger specific studies (serologies, PCR).

Background & Introduction

- Respiratory infections

Infections related to conditioning regimen and neutropenia

Day 0 to day 30

Pulmonary oedema

Pleural effusion

Transfusion-related acute lung injury

Idiopathic pneumonia syndrome

Engraftment syndrome

Diffuse alveolar haemorrhage

Aspergillosis

Candidaemia (*Candida* sepsis) and candidiasis (general *Candida* infections)

Respiratory viruses – Respiratory syncytial virus, parainfluenza, influenza

Bacteraemias of gastrointestinal origin

Infections of central venous catheter origin

Acute respiratory distress syndrome (ARDS)

Chemotherapy-associated pulmonary toxicity

The European Blood and Marrow Transplantation Textbook for Nurses. Springer, Cham

Background & Introduction

- Respiratory infections

Classic opportunistic infections

Day 31 to day 100

Pulmonary veno-occlusive disease (due to hepatic sinusoidal obstructive

Syndrome)

Diffuse alveolar haemorrhage

Cytomegalovirus

Aspergillosis

Pneumocystis carinii pneumonia

Respiratory viruses – Respiratory syncytial virus, parainfluenza, influenza

Toxoplasmosis

ARDS

Idiopathic pneumonia syndrome

Chemotherapy-associated pulmonary toxicity

The European Blood and Marrow Transplantation Textbook for Nurses. Springer, Cham

Background & Introduction

- Respiratory infections

Infections from encapsulated organisms	Aspergillosis
Greater than day 100	Respiratory viruses – Respiratory syncytial virus, parainfluenza, influenza
	Varicella zoster virus
	Cytomegalovirus
	Pneumocystis carinii pneumonia
	Post-transplant lymphoproliferative disorder
	Pneumonia
	ARDS
	Bronchiolitis obliterans
	Bronchiolitis obliterans organizing pneumonia
	Chemotherapy-associated pulmonary toxicity

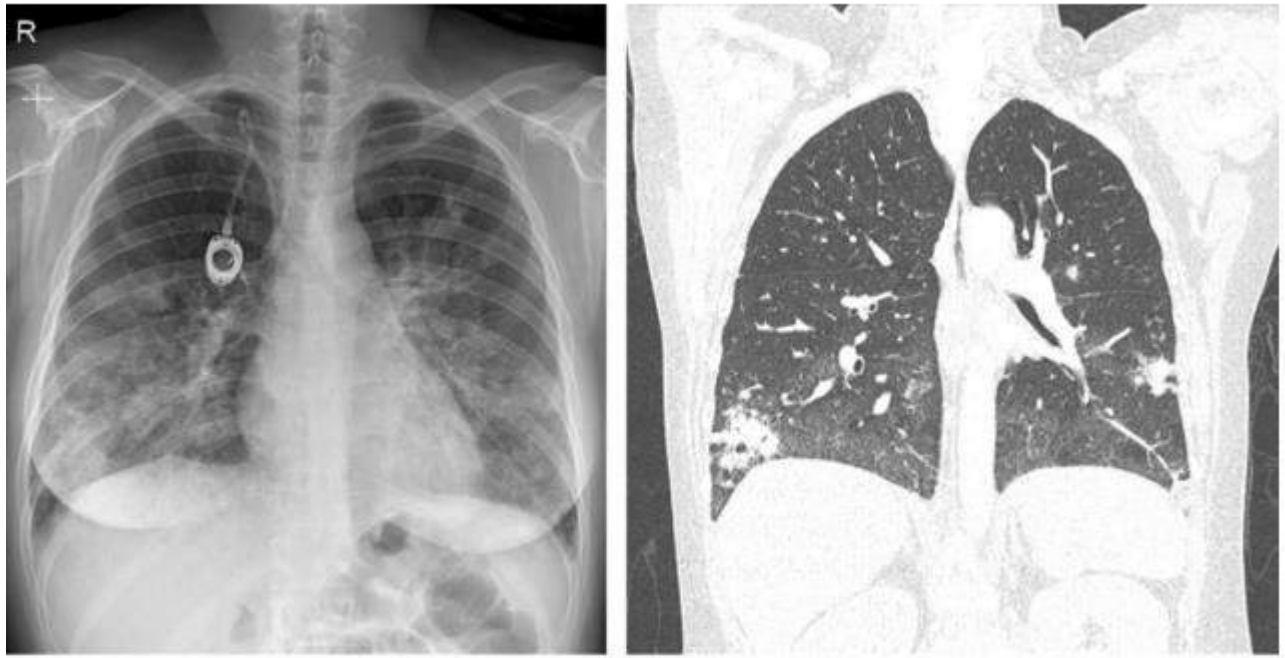
The European Blood and Marrow Transplantation Textbook for Nurses. Springer, Cham

Background & Introduction

- Respiratory infections

  The **differential diagnosis** of pulmonary opacities in patients with hematologic malignancies is broad and includes both infectious and noninfectious causes.

  • Pneumonia, pulmonary hemorrhage, edema, and leukostasis, are well-known and common acute pulmonary complications in these patients.



Respiratory syncytial virus–related pneumonia in a patient who underwent autologous HSCT

Background & Introduction

- Fungal infections

Fungal infection is a common cause of pneumonia in neutropenic patients after chemotherapy or HSCT, and the most common fungal pathogen is **Aspergillus.**

- Although **Aspergillus infection** commonly occurs in the neutropenic phase during the first 30 days after HSCT, the transplant recipient may be in danger of invasive aspergillosis throughout the period of immunosuppression.

- Graft-versus-host disease and corticosteroid use are risk factors for late-onset invasive aspergillosis.

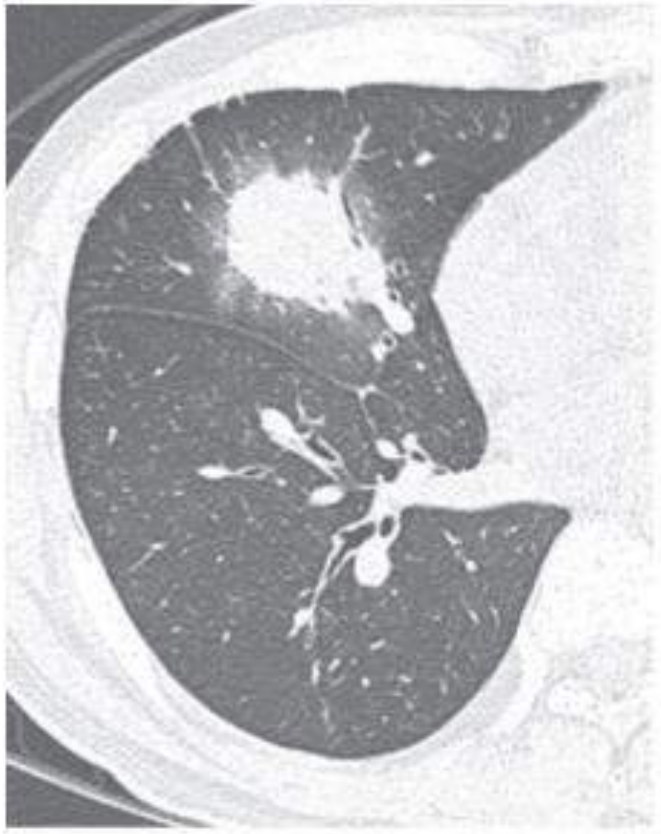
Principles and Practice of Pediatric Infectious Diseases: 4th Edition

Evidenced based practice & Indications

- Fungal infections.

Diagnosis

- Fever, pleuritic chest discomfort, dyspnea.
- Imaging shows nodules or cavitating infiltrates.
- The classic “halo sign” may be seen on chest CT, but imaging may not be helpful.
- A BAL may be useful.
- **Galactomannan** (twice a week) and beta-glucan testing may be helpful but are not always informative.



Chest CT image obtained in a patient with CML shows an ovoid area of consolidation with surrounding ground-glass opacities (halo sign), findings suggestive of invasive pulmonary aspergillosis

The European Blood and Marrow Transplantation Textbook for Nurses. Springer, Cham

Evidenced based practice & Indications

- Fungal infections

Prevention

- **Early post- transplant period** is:
- Equipping the HSCT rooms with High-efficiency filters (HePa)

  (avoid the dissemination of airborne Aspergillus spores into the room)
- **After discharge from the HSCT room:**
- Posaconazole or voriconazole is highly recommended in the late or very late period.
- Especially in the presence of GvHD.

www.hospitalpharmacyeurope.com

Evidenced based practice & Indications

- Fungal infections

  Treatment

  - **Most effective** antifungals for Aspergillosis are:
    - Voriconazole, liposomial Amphotericina B or Isavuconazole (6-12 weeks)
  - **Second- line** therapy in patients no responsive after 7-14 days :
    - Caspofungin or Posaconazole.
  - The combination of antifungal drugs with a synergistic mechanism of action, is reserved for refractory episodes.

www.hospitalpharmacyeurope.com

Evidenced based practice & Indications

- Fungal infections. **P jirovecii**

➢The primary infections is usually asymptomatic or may cause only mild upper respiratory tract disease.

➢In severely immunocompromised patients may cause Pneumonia (PjP) mortality rate up 50 %

➢Primary prophylaxis with trimethoprim/ sulfamethoxazole is highly effective

➢Dapsone is a valid alternative for preventing PCP in adult HSCT recipients who are intolerant of trimethoprim/sulfamethoxazole

J Antimicrob Chemother 2016; 71: 2397–2404

Evidenced based practice & Indications

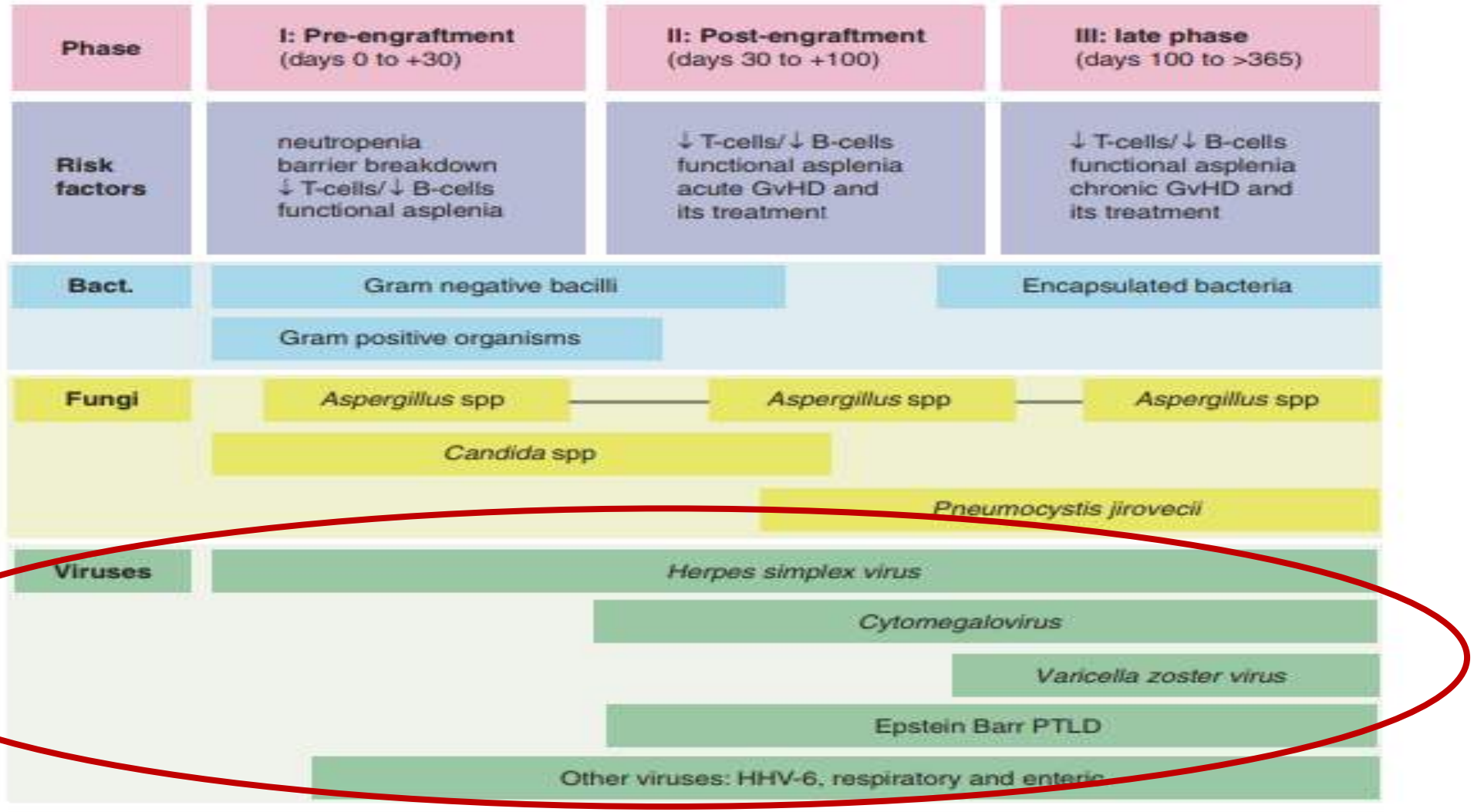


Fig. 7.2 Chronology of predominant infections after HSCT (Adapted from [1] and granted permission from (EBMT Handbook 2012))

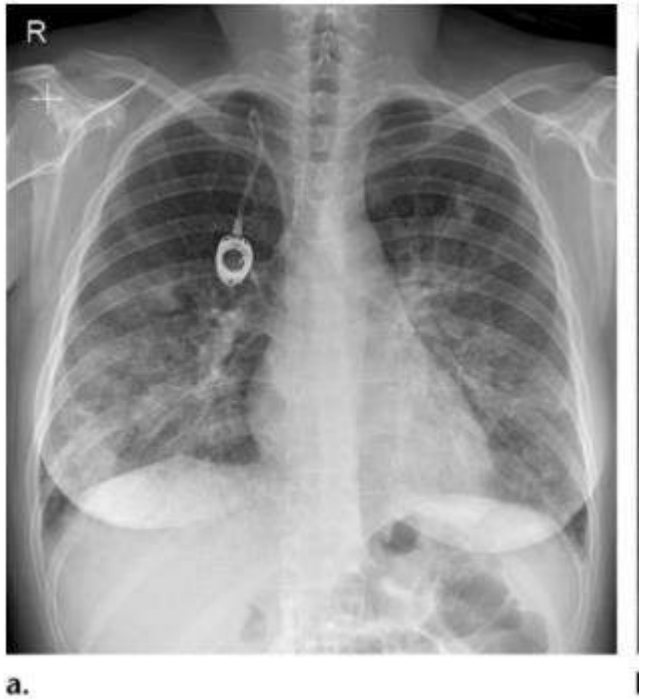
Background & Introduction

- Common viral complications. **Viral pneumonia**

  ❖ Pulmonary infections of viral origin are also associated with high rates of morbidity and mortality among patients with hematologic malignancies.

  ❖ Although CMV infection is the most common cause of viral pneumonia

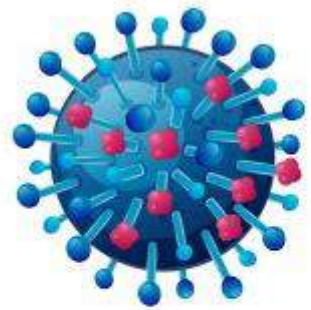
  ❖ Other respiratory viruses (rhinoviruses, adenoviruses, influenza viruses, parainfluenza viruses, respiratory syncytial virus, metapneumovirus) also have been identified with recently developed molecular based diagnostic tools.



Respiratory syncytial virus–related pneumonia in a patient who underwent autologous HSCT

RG • Volume 34 Number 6 Choi et al 1763

Background & Introduction



Influenza

- Common viral infections

Viral complications in HSCT patients may be classified in :

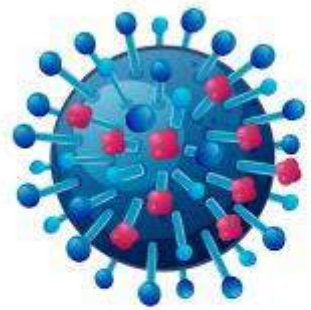
1.- Community- acquired respiratory viral infections (CARVI)

2.- Viral infections due to **reactivations** of a latent virus previously acquired by the patients or by the **donors** and transmitted to the patients by the graft cells.

Responsible for **upper respiratory** tract infection and higher incidence of lower respiratory tract infections, pneumonia and respiratory insufficiency.

www.hospitalpharmacyeurope.com

Background & Introduction



Influenza

- Common viral infections

1.- Community- acquired respiratory viral infections (CARVI)

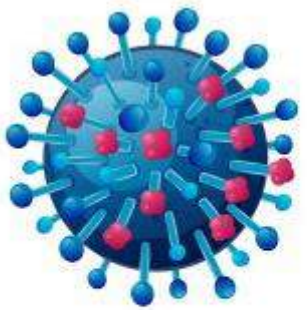
(adenoviruses, influenza viruses, parainfluenza viruses, respiratory syncytial virus)

✓ May occur in any phase after HSCT

✓ **Key prevention policy :**

- avoid contact with people who are affected or incubating
- patient isolation
- education and strict control of family members, health personnel or providers.

Background & Introduction



Influenza

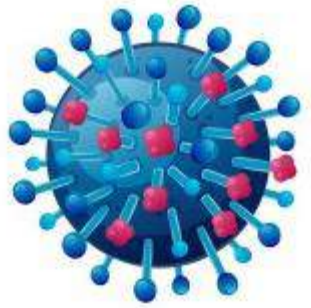
- Common viral infections

2.- Viral infections due to **reactivations of a latent virus** previously acquired by the patients or by the donors.

- Re-exacerbation of mucocutaneous HSV infection that can worsen post chemo . mucositis.
- Prophylaxis and therapy based in IV Aciclovir
- Foscarnet or cidofovir are the alternative therapeutic choices.

www.hospitalpharmacyeurope.com

Background & Introduction

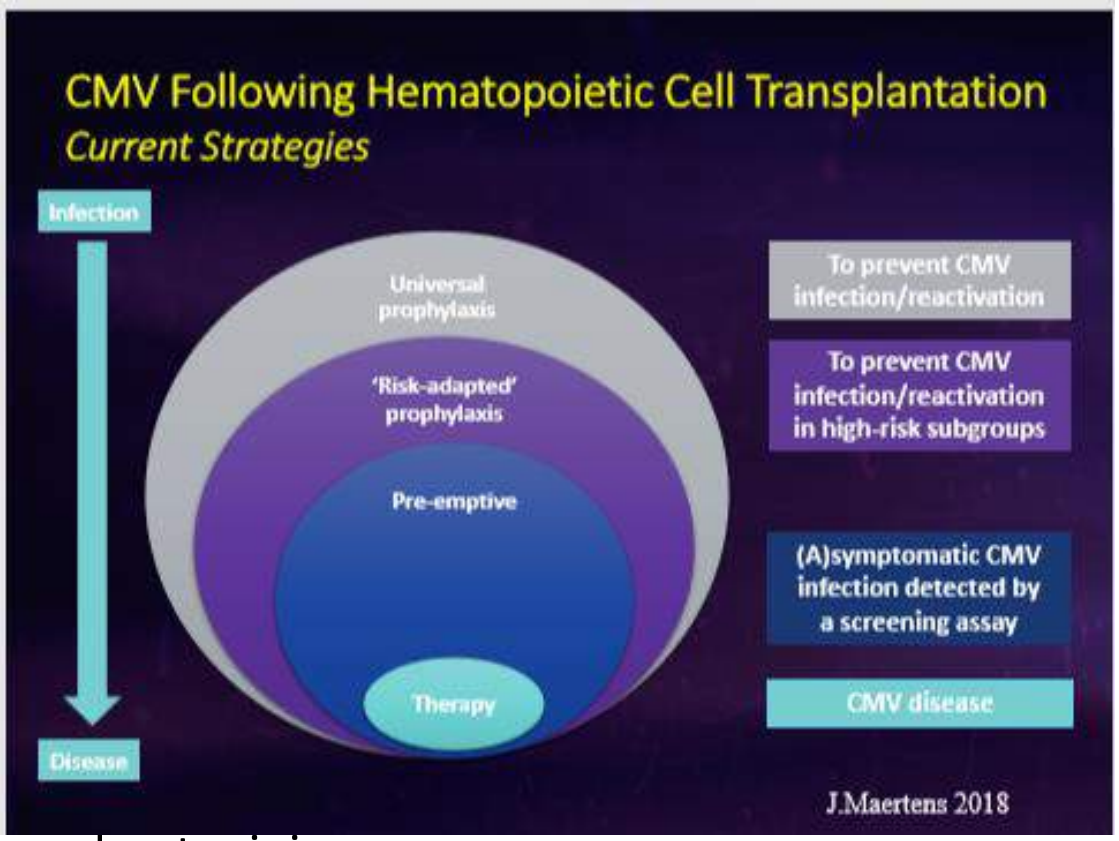


Influenza

- Common viral infections . **CMV**
- **CMV** infection observed in 30-60 % of allogeneic HSCT
- **CMV pneumonia** characterised by :
  - Fever
  - Tachypnea
  - Hypoxemia
  - Non-productive cough → respiratory insufficiency
- **CMV enteritis ,** characterized by:
  - Diarrhea
  - With or without low grade fever

Background & Introduction

- Common viral infections . **CMV**
- **CMV prophylaxis (** positivity of recipient or the donor)
- For the first 100 days , ganciclovir…..valganciclovir…
- Weekly monitoring of blood CMV load by PCR
- and prompt starting antiviral treatment



- **CMV treatment**
- Ganciclovir (10 mg/kg/day)
- Foscarnet (120-180 mg/kg/ day)

} IV 2 weeks at minimum

Background & Introduction

- Common viral infections. **BKPyV**
  - Acquired during infancy and latent in the uroepithelial layer of kidney and bladder mucosa
    - Viuria and/or viraemia associated with symptomatic
    - **hemorrhagic cystitis** (macro-haematuria, dysuria, pain)
  - **Supportive measures:**
    - parenteral hyperhydration
    - platelet and blood transfusions,
    - bladder irrigation
    - analgesic
  - **Treatment** : Cidofovir

Conclusion

- Nursing care for pulmonary complication
  - Nurses are the most likely to observe subtle changes in the patient's condition, and for this reason it is critical that nursing staff working with the HSCT population be **highly trained** in oncology and critical care interventions
  - Clinical nurses at the forefront of identifying and reporting suspicious symptoms to the healthcare team (Mattson, 2007). Nurses take a central role in **patient and family education** regarding the course of **treatment, complications**, and other key pieces of the HSCT process, including caring for a central line
  - Nurses ensure patient participation in **identifying developing complications** early and improving HSCT outcomes.
  - When assessing for pulmonary complications in a post-transplant patient, frequent and careful nursing **assessment of laboratory work and weight changes** with a focus on the cardiopulmonary systems are customary
  - Vital signs, including the rate and quality of respirations, and oximetry should be performed per program protocols, usually every four hours and more frequently for patients at risk for pulmonary insufficiency.

Background & Introduction

- Multi-resistant bacteria – reducing the spread
- **Incidence** of bacterial infections is higher during the early pre-engraftment period .
- Saprophyte bacteria from non- sterile sites to the body (mouth, intestine , skin) to the blood : oral mucositis, severe neutropenia or CVC.
- **Aetiology** is radiological-ultrasound documented only in the 20-30f episodes.
- 50% of episodes are classified as fever of unknow origin (FUO)
- Most frequent aetiologic agents are:

❖ Gran positive bacteria specially coagulase –negative

❖ Intestinal gran-negative bacteria such *Escherichia coli, Pseudomonas spp, Klebsiella spp. Serratia and Enterobacter*

Background & Introduction

- Multi-resistant bacteria – reducing the spread
- **Diagnosis** : at the spiking of fever the essential

diagnostic work –up includes:

- ❑Blood culture : - peripheral vein and CVC.
- ❑Urine and stool cultures
- ❑Culture or swab from any suspected site of infections.
- ❑Blood cells count
- ❑Biochemical analysis (C- reactive protein and / procalcitonin)
- ❑Imaging investigation according to any clinical suspition.

Evidenced based practice & Indications

- Multi-resistant bacteria – reducing the spread
- **Early pre-engraftment period : Prevention**
- Hygiene measures:
  - hand washing, oral hygiene.
  - low bacterial diet (always controversial)
  - **adults:** antibacterial prophylaxis with oral fluoroquinolones (ciprofloxacin, levofloxacin)

Evidenced based practice & Indications

- Multi-resistant bacteria – reducing the spread
- **Early pre-engraftment period : Treatment**

Every febrile episode in this period has to be treated immediately and empirically with a broad spectrum antibiotic to cover the most frequents pathogens !!!!!

- First line empirical antibiotics monotherapy with either piperacillin-tazobactam or ceftazidime, cefepime
- Second line
  - Cellulitis, pneumonia, mucositis…….. vancomycin or teicoplanin
  - Abdominal cramps, typhlitis …….metronidazole.

Evidenced based practice & Indications

- Multi-resistant bacteria – reducing the spread
- **Late and very late phase infection**
- Mostly due to encapsulated bacteria (*Streptococcus pneumonia, Haemophilus influenzae)*
- Due to chronic GvHD:

  - prevention :vaccination for encapsulated bacteria (start 3 or 6 months after HSCT)
  - periodic IV IgG (serum level above 4g/dl.)
  - antibiotics prophylasis with penicillin

Evidenced based practice & Indications

- Multi-resistant bact
- Standard precautio

Standard precautions	Standard pr transmissio non-intact s to be used w infectious o	es used to prevent ith blood, body fluids, es. These measures are or not they appear
Hand hygiene	Hand hygie and to the u soiled, alcoh healthcare t	cterial soap and water en hands are not visibly e when providing

(https://www.dhs.wisconsin.gov/ic/precautions.htm)

Evidenced based practice & Indications

- Multi-resistant bacteria – reducing the spread
- Standard precautions of infection control

Personal protective equipment (PPE)	PPE includes items such as gloves, gowns, masks, respirators and eyewear protectors used to create barriers that protect the skin, clothing, mucous membranes and the respiratory tract from infectious agents PPE is used as a last resort when work practices and engineering controls alone cannot eliminate worker exposure The items selected for use depend on the type of interaction a public health worker will have with a client and the likely modes of disease transmission Wear gloves when touching blood, body fluids, non-intact skin, mucous membranes and contaminated items. Gloves must always be worn during activities involving vascular access, such as performing phlebotomies Wear a surgical mask and goggles or face shield if there is a reasonable chance that a splash or spray of blood or body fluids may occur to the eyes, mouth or nose Wear a gown if skin or clothing is likely to be exposed to blood or body fluids remove PPE immediately after use and wash hands. It is important to remove PPE in the proper order to prevent contamination of skin or clothing

(https://www.dhs.wisconsin.gov/ic/precautions.htm)

Evidenced based practice & Indications

- Multi-resistant bacteria – reducing the spread
- Standard precautions of infection control

Needle stick and sharp injury prevention	Safe handling of needles and other sharp devices is a component of standard precautions that are implemented to prevent healthcare worker exposure to blood-borne pathogens. The Needlestick Safety and Prevention Act (link is external) mandates the use of sharps with engineered safety devices when suitable devices exit
Cleaning and disinfection	Client care areas, common waiting areas and other areas where clients may have potentially contaminated surfaces or objects that are frequently touched by staff and clients (doorknobs, sinks, toilets other surfaces and items in close proximity to clients) should be cleaned routinely with EPA-registered disinfectants, following the manufacturer's instructions for amount, dilution and contact time

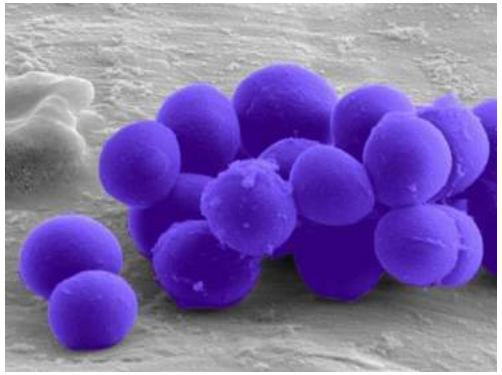
(https://www.dhs.wisconsin.gov/ic/precautions.htm)

Evidenced based practice & Indications

- Multi-resistant bacteria – reducing the spread. Standard precautions of infection control (https://www.dhs.wisconsin.gov/ic/precautions.htm)

Respiratory hygiene (cough etiquette)	Clients in waiting rooms or other common areas can spread infections to others in the same area or to local public health agency staff. Measures to avoid spread of respiratory secretions should be promoted to help prevent respiratory disease transmission. Elements of respiratory hygiene and cough etiquette include: Covering the nose/mouth with a tissue when coughing or sneezing or using the crook of the elbow to contain respiratory droplets Using tissues to contain respiratory secretions and discarding in the nearest waste receptacle after use Performing hand hygiene (handwashing with non-antimicrobial soap and water, alcohol-based hand rub or antiseptic handwash) immediately after contact with respiratory secretions and contaminated objects/materials Asking clients with signs and symptoms of respiratory illness to wear a surgical mask whilst waiting in common areas or placing them immediately in examination rooms or areas away from others. Provide tissues and no-touch receptacles for used tissue disposal Spacing seating in waiting areas at least three feet apart to minimize close contact among persons in those areas

Evidenced based practice & Indications



- Multi-resistant bacteria – reducing the spread.
- **Methicillin-resistant S. aureus (MRSA)**

Insufficient evidence to recommend:

Routine screening

Use of topical or systemic antimicrobial therapy for asymptomatic MRSA colonization

If high rates of MRSA, consider **adjunctive strategies**:

implementing a program to obtain MRSA surveillance cultures on admission and serially (weekly) (BII)

decolonization therapy (BIII)

routine bathing of patients with chlorhexidine (BIII)

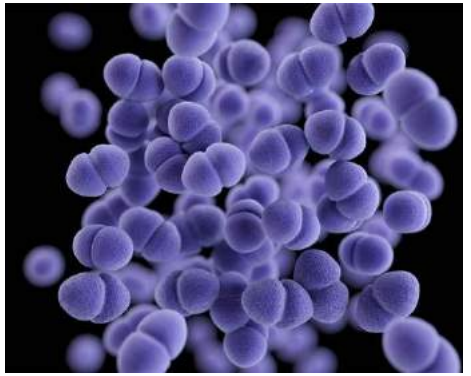
The optimal duration of contact precautions for patients with MRSA is unknown.

Possible **discontinuation criteria** (CIII):

-contact precautions until all antimicrobials active against the MRSA isolate are discontinued

-three consecutive screening cultures taken on separate days are negative

Evidenced based practice & Indications



- Multi-resistant bacteria – reducing the spread.

Vancomycin-resistant enterococcus (VRE)

- Minimize use/duration of vancomycin treatment

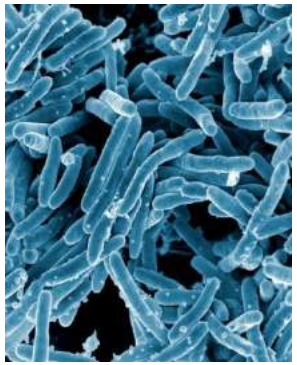
- **contact precautions** in case of readmissions

- VRE rectal or stool **active surveillance cultures** to identify colonized patients if evidence for ongoing transmission of VRE in an HCT unit

- Possible **discontinuation criteria**

-contact precautions until all antimicrobials active against the VRE are discontinued
-three consecutive screening cultures taken on separate days are negative

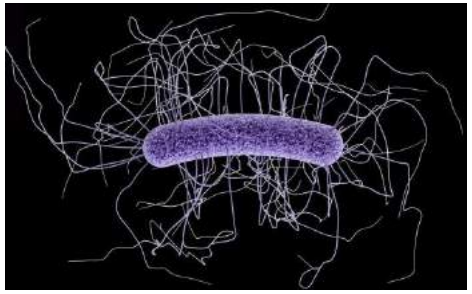
Evidenced based practice & Indications



- Multi-resistant bacteria – reducing the spread.
- **Multidrug-resistant Gram-negative bacilli (GNB)**

  - Effectiveness of **active surveillance-culturing** (ASC) program for MDR-GNB is unknown
  - Units experiencing high rates of MDR-GNB infection can consider the use of ASC as a component of their control and prevention program

Evidenced based practice & Indications



- Multi-resistant bacteria – reducing the spread.
- **Clostridium difficile**

❖ **Contact precautions** for the duration of illness and until the patient is asymptomatic

If evidence of ongoing transmission of C.difficile consider maintaining contact precautions even after diarrhea has resolved and until hospital discharge

Hand hygiene by soap and water

A '**test of cure**' is discouraged

❖ Practices Not Recommended :

Routine stool surveillance cultures or toxin assays for C. difficile among asymptomatic patients or HCWs, even during outbreaks .

Culturing the hand swabs of HCWs for C. difficile

Treating asymptomatic C. difficile carriers to prevent clinical infection

Evidenced based practice & Indications

Empirical Contact + Droplet precautions

Pathogen-specific CRV isolation precautions

Contact precautions for RSV and parainfluenza.
Droplet precautions for influenza.
Droplet + contact precautions for adenovirus.
Airborne + contact precautions for primary or disseminated varicella infection.

Precautions for at least the duration of illness and continued for the duration of hospitalization or viral shedding

HCWs with URI symptoms should be reassigned to non-patient care duties until symptoms resolve

Visitors with URI symptoms should be asked to defer their visit to the HCT center until their URI symptoms resolve

HCWs and visitors with **infectious conjunctivitis** should be restricted from direct patient contact until the drainage resolves

Conclusion

- Infections are a major cause of morbidity and mortality in allogeneic transplantation

- Therefore, it is crucial to have a **skilled nursing team** to assess, prevent, detect and treat infections.

- Delays in diagnosing an infection that results from a depressed inflammatory response may lead to increased susceptibility to a broad range of potentially life-threatening organisms.

- For this reason, in addition to antimicrobial prophylaxis, there are other important strategies to prevent infections, for example, building a **multi-professional network** team specialized in infection control measures

The European Blood and Marrow Transplantation Textbook for Nurses. Springer, Cham

Conclusion

- **Protective environment for haematopoietic cell transplant recipients**

❖A protective environment plays a key role in ensuring the safety of patient after transplant (propose a range of responsibilities for the transplant team in order to ensure they possess sufficient knowledge about what this entails)

Protective environment for haematopoietic cell transplant recipients J. Styczynski et al.

Protective Environment rooms that incorporate the following features:

- >12 air exchanges/h
- HEPA filters with a 99.97% efficiency for removing particles >0.3 lm (AIII)
- directed air flow (BIII)
- positive air-pressure differential (Pa) between the room and the hallway >2.5 Pa (BIII)
- self-closing doors (BIII)

Priority order for the more at-risk patients (e.g., expected prolonged neutropenia, receiving treatment for GVHD) (BIII)

Conclusion

- **Protective environment for haematopoietic cell transplant recipients**

❖It should be noted that daily check-up performed by physicians, nurses and cleaning staff is based on routine activity and does not require additional work, except when reporting failures in the system.

❖ A meeting of transplant ward personnel and hospital technical personnel responsible for environmental services is recommended once a year.

❖ In parallel, hospital infection control group should implement and run program of epidemiology, prophylaxis and management of infections in transplant unit.

Conclusion

Protective environment for haematopoietic cell transplant recipients

- ❑All HCWs with diseases transmissible by direct contact, droplet or airborne transmission should be **restricted** from direct **patient contact** and temporarily reassigned to other tasks
- ❑**Work exclusion policies** should be designed
- ❑Published recommendations regarding the **duration of work restrictions** should be followed
- ❑**Immunization** of all HCWs with all recommended vaccines. Prefer inactivated vaccines, if possible
- ❑Annual vaccination for influenza
- ❑Written comprehensive **policy regarding immunizations and vaccinations** for HCT employees that meets current Infection Control Guidelines

Conclusion

Protective environment for haematopoietic cell transplant recipients

Preventing Opportunistic Infections After Hematopoietic Stem Cell Transplantation: The Centers for Disease Control and Prevention, Infectious Diseases Society of America, and American Society for Blood and Marrow Transplantation Practice Guidelines and Beyond

Keith M. Sullivan, Clare A. Dykewicz, David L. Longworth, Michael Boeckh, Lindsey R. Baden, Robert H. Rubin, and Kent A. Sepkowitz

GUIDELINES

Infection prevention and control in health-care facilities in which hematopoietic cell transplant recipients are treated

D Yokoe[1], C Casper[2], E Dubberke[3], G Lee[4], P Muñoz[5], T Palmore[6], K Sepkowitz[7], J-AH Young[8] and JP Donnelly[9]

Conclusion

- **B2: CLINICAL UNIT B2.1**

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contami

B2: CLINICAL UNIT

STANDARD:

B2.1 *There shall be a designated inpatient unit of appropriate location and adequate space and design that minimizes airborne microbial contamination.*

Explanation:

Clinical unit facilities may vary among centers. Variability may reasonably be based on a number of factors, including the number and/or type (autologous or allogeneic) of transplants performed, the patient case mix, the graft source, epidemiological factors influencing the prevalence of opportunistic infections, potential economic factors, and an increasing use of ambulatory facilities for transplantation.

This standard is not meant to imply that every clinical unit must have laminar airflow available, but HEPA filtration with positive pressure is recommended for high risk patients. If non-HEPA filtered rooms are used for lower risk patients or if there is a shortage of HEPA filtered rooms, the SOP(s) on infection control, biosafety, and chemical and radiological safety should indicate how allocation of rooms is prioritized. Further, auditing of airborne microbial infections in non-HEPA rooms should be performed as part of the QM Program.

Conclusion

B3.7 NURSES

B3.7.1 The Clinical Program shall have nurses formally trained and experienced in the management of patients receiving cellular therapy.

B3.7.2 Clinical Programs treating pediatric recipients shall have nurses formally trained and experienced in the management of pediatric patients receiving cellular therapy.

B3.7.3 Nurses shall have received specific training and maintain competence in the transplant-related skills that they routinely practice including:

B3.7.3.4 Care interventions to manage cellular therapy complications, including, but not limited to, cytokine release syndrome, tumor lysis syndrome, cardiac dysfunction, respiratory distress, neurologic toxicity, macrophage activation syndrome, renal and hepatic failure, disseminated intravascular coagulation, anaphylaxis, neutropenic fever, infectious and noninfectious processes, mucositis, nausea and vomiting, and pain management.

Literature reference

Respiratory infections

1.-Trasnspl Infect Dis. 2018 Jun;20(3):e12882. doi: 10.1111/tid.12882. Epub 2018 Apr 2.
A multicenter investigation of respiratory syncytial viral infection in children with hematopoietic cell transplantation.
Rowan CM[1], et al; Hematopoietic Cell Transplant group of the Pediatric Acute Lung Injury and Sepsis Investigator (PALISI) network.

2**.-Acute Pulmonary Complications in Patients with Hematologic Malignancies** . Moon Hyung Choi, MD et al. RadioGraphics 2014; 34:1755–1768

3.-**Survey of CMV management in pediatric allogeneic HSCT programs, on behalf of the Inborn Errors, Infectious Diseases and Pediatric Diseases Working Parties of EBMT.** T Bontant et al. Bone Marrow Transplantation (2014) 49, 276–279; doi:10.1038/bmt.2013.164; published online 28 October 2013

4**.-Viral Respiratory Tract Infections in Allogeneic Hematopoietic Stem Cell Transplantation Recipients in the Era of Molecular Testing.**
Sim SA[1], et al. Biol Blood Marrow Transplant. 2018 Jul;24(7):1490-1496. doi: 10.1016/j.bbmt.2018.03.004. Epub 2018 Mar 9.

5.-**Background to hematopoietic cell transplantation, including post transplant immune recovery.** Mackall C[1], Bone Marrow Transplant. 2009 Oct;44(8):457-62. doi: 10.1038/bmt.2009.255.

6.-**ECIL guidelines for preventing Pneumocystis jirovecii pneumonia in patients with haematological malignancies and stem cell transplant recipients.** Maertens J[1] J Antimicrob Chemother. 2016 Sep;71(9):2397-404. doi: 10.1093/jac/dkw157. Epub 2016 May 12

7.- **Pulmonary infections after bone marrow transplantation: high-resolution CT findings in 111 patients.** Escuissato DLAJR Am J Roentgenol. 2005 Sep;185(3):608-15
.

8.- Murray J., Agreiter I., Orlando L., Hutt D. (2018) **BMT Settings, Infection and Infection Control**. In: Kenyon M., Babic A. (eds) The European Blood and Marrow Transplantation Textbook for Nurses. Springer, Cham

Literature reference

9.-Julie Delaloye and Thierry Calandra* Invasive candidiasis as a cause of sepsis in the critically ill patient. Virulence 5:1, 161–169; January 1, 2014; © 2014 Landes Bioscience

BMT setting Infections

1.-Tomblyn, M., Chiller, T., Einsele, H., Gress, R., Sepkowitz, K., Storek, J., … Boeckh, M.J. (2009). Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: A global perspective. Biology of Blood and Marrow Transplantation, 15, 1143–1238. doi:10.1016/j.bbmt.2009.06.019

2.-Parody R, Martino R, Rovira M, Vazquez L, Vázquez MJ, De la Cámara R, Blazquez C, Fernández-Avilés F, Carreras E, Salavert M, Jarque I, Martín C, Martínez F, López J, Torres A, Sierra J, Sanz GF, Infectious/Non-infectious Complications Subcommittee of the Grupo Español de Trasplante Hematopoyético (GETH. Severe infections after unrelated donor allogeneic hematopoietic stem cell transplantation in adults: comparison of cord blood transplantation with peripheral blood and bone marrow transplantation. Biol Blood Marrow Transplant. 2006;12:734–48.

3.-. Jan Styczynski1 ● Gloria Tridello2 ● J. Peter Donnelly3 ● Simona Iacobelli4 ● Jennifer Hoek5 ● Malgorzata Mikulska6 ● Mahmoud Aljurf7 ● Lidia Gil8 ● Simone Cesaro2Protective environment for hematopoietic cell transplant (HSCT) recipients: The Infectious Diseases Working Party EBMT analysis of global recommendations on health-care facilities .**Bone Marrow Transplantation (2018) 53:1131–1138 https://doi.org/10.1038/s41409-018-0141-5**

Conclusion

Thanks you

"Don't think of it as getting a flu shot.
Think of it as installing virus protection software."

Supportive Care of HSCT

Marta Canesi, Italy

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

Supportive care: principles

The provision of the necessary services for those affected by cancer or undergoing HSCT to **meet their physical, emotional, social, psychological, informational, spiritual and practical needs** during the diagnostic, treatment and follow-up phases, encompassing issues of survivorship, palliative care and bereavement.

GOAL: Supportive care can prevent or reduce the effects related to transplant.

Nurses can provide effective supportive care by:

- Reducing the risk of developing unmet needs early
- Detecting unmet needs early
- Implementing intervention to promote supportive care, even at the end of life
- Timely referral to other professionals or services if required.

Why is it important?

Early identification and referral of individuals with unmet supportive care needs can improve **outcomes** like:

- Patient level of stress
- Likelihood of developing clinical anxiety and depression
- Quality of life
- Patient satisfaction
- Communication with the health care team
- Adherence to treatment
- Cost and usage of health care system

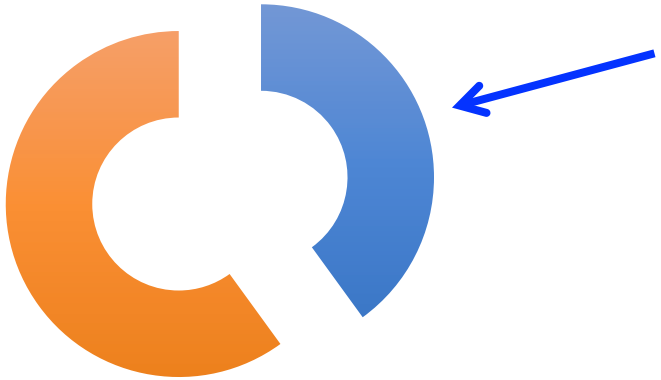
UNMET SUPPORTIVE CARE NEEDS → **Morbidity and Distress**

Unpleasant emotional experience of a psychological, social and/ or spiritual nature that may interfere with the ability to cope effectively with the severe clinical conditions during and after transplant.

It can be represented by **feelings of** vulnerability, sadness, fears and also **disabling problems** like depression, anxiety, panic, social isolation, existential and spiritual crisis.

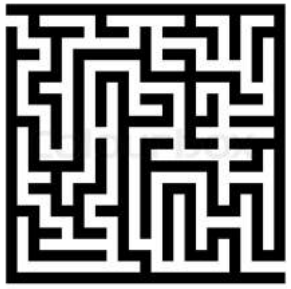
Emotional distress is most intense before HSCT and gradually resolves over the next 2 to 5 years.

50% of those undergoing HSCT are depressed. This increased the mortality rate and reduce the quality of life.



40% of patients post- HSCT present
-depression
-anxiety
-posttraumatic stress disorders

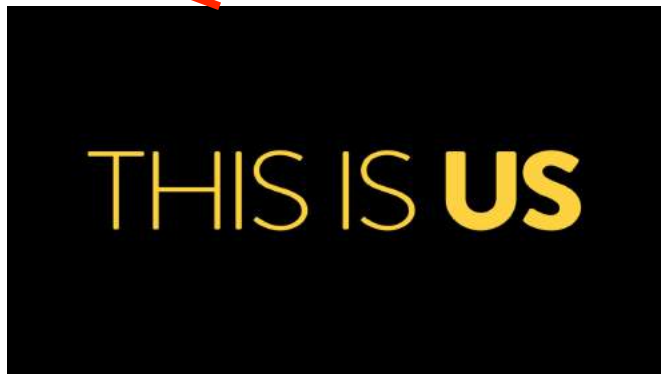
Several unmet needs are psychological but patient is lost.



Around 50% of patients are referred for psychological help despite having needs identified.

Lack of Follow-up

- **Inappropriate time OF referrals**
- **Health Professionals**
  - Not knowing about available supportive care resources
  - Not asking about supportive care needs
  - Not able to introduce the supportive care service properly



Who is at risk?

INDIVIDUAL factors

1. Extreme ages (older and younfer)
2. Living alone − absence of a partner (single, divorced, widowed)
3. Poor marital functioning
4. History of substance/alchool abuse
5. Economic burden
6. Absence or perception of poor social support
7. Past psychiatric treatment (depression!!)
8. Overall stressful life events

Who is at risk?

DISEASE/ TREATMENT factors

1. Diagnosis and recurrence
2. Poor prognosis
3. Severe and multiple treatment effects
4. Type of transplant
5. Chronic pain
6. Fatigue
7. Greater functional impairment, disease burden
8. Complications and GVHD

Risk factors related to transplant experience include

- Severe experience of transplantation
- Allogeneic transplant
- Not the gender (generally females are at higher risk but not in transplanted patients)
- Emotional health status right before and after transplantation

How to measure the emotional distress?

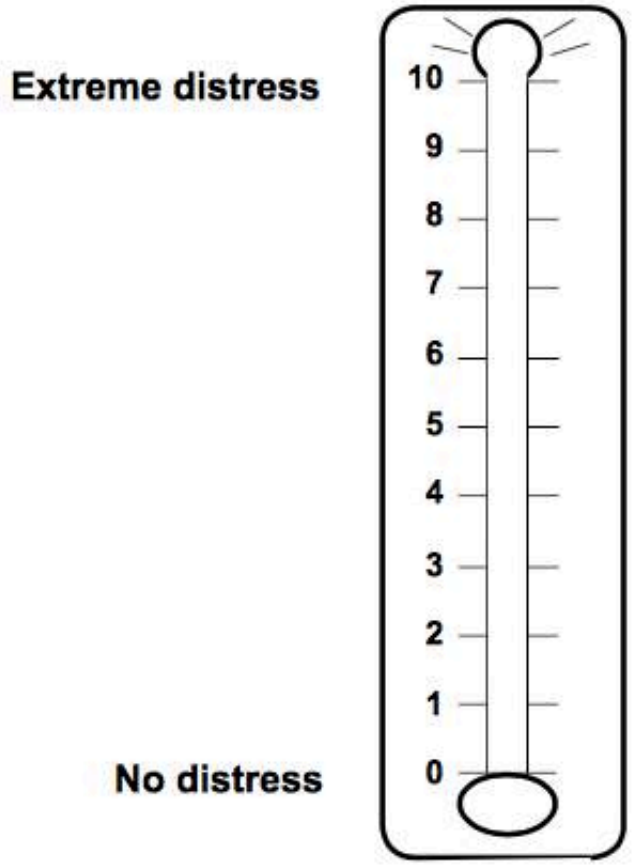
DISTRESS THERMOMETHER
NATIONAL COMPREHENSIVE CANCER NETWORK

Opportunity for the patient to begin talking about and labeling the lived exeriences and emotions.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3445407/pdf/nihms389468.pdf

NCCN DISTRESS THERMOMETER

Instructions: Please circle the number (0–10) that best describes how much distress you have been experiencing in the past week including today.



PROBLEM LIST

Please indicate if any of the following has been a problem for you in the past week including today.

Be sure to check YES or NO for each.

YES	NO	Practical Problems
❑	❑	Child care
❑	❑	Housing
❑	❑	Insurance/financial
❑	❑	Transportation
❑	❑	Work/school
❑	❑	Treatment decisions
		Family Problems
❑	❑	Dealing with children
❑	❑	Dealing with partner
❑	❑	Ability to have children
❑	❑	Family health issues
		Emotional Problems
❑	❑	Depression
❑	❑	Fears
❑	❑	Nervousness
❑	❑	Sadness
❑	❑	Worry
❑	❑	Loss of interest in usual activities
❑	❑	**Spiritual/religious concerns**

YES	NO	Physical Problems
❑	❑	Appearance
❑	❑	Bathing/dressing
❑	❑	Breathing
❑	❑	Changes in urination
❑	❑	Constipation
❑	❑	Diarrhea
❑	❑	Eating
❑	❑	Fatigue
❑	❑	Feeling swollen
❑	❑	Fevers
❑	❑	Getting around
❑	❑	Indigestion
❑	❑	Memory/concentration
❑	❑	Mouth sores
❑	❑	Nausea
❑	❑	Nose dry/congested
❑	❑	Pain
❑	❑	Sexual
❑	❑	Skin dry/itchy
❑	❑	Sleep
❑	❑	Substance use
❑	❑	Tingling in hands/feet

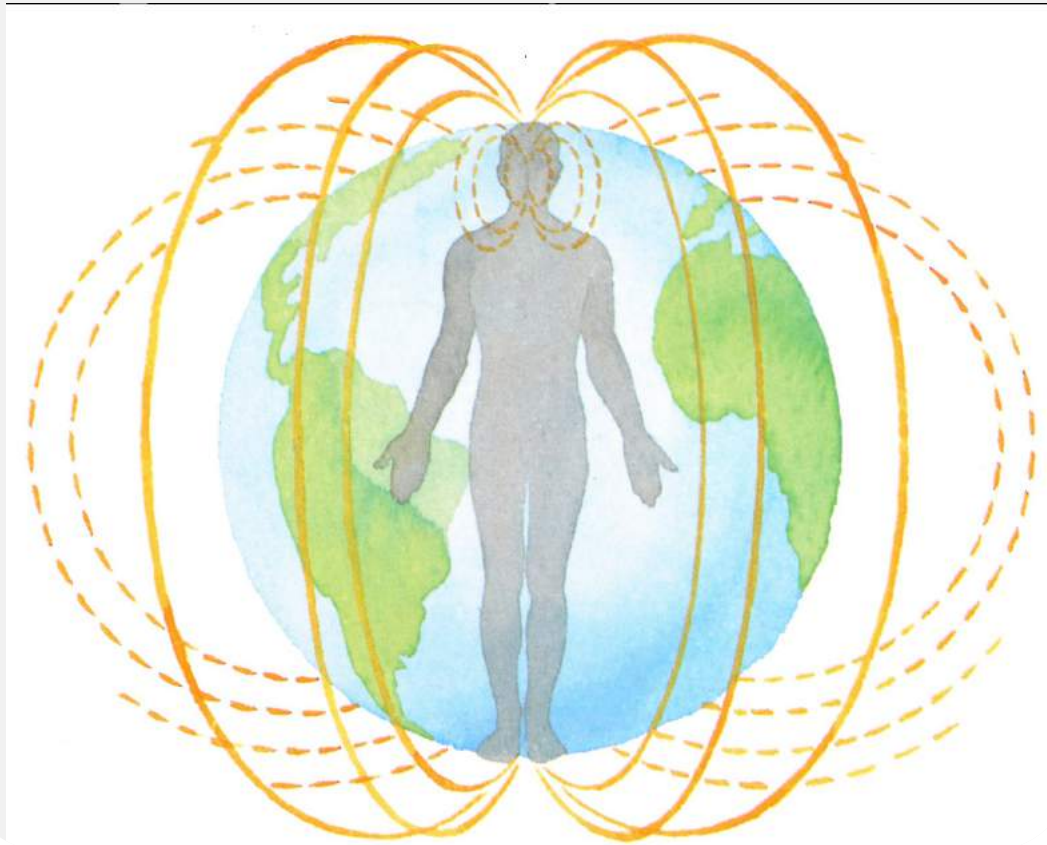
Other Problems: _____

_____

AREAS OF INTEREST

Assess specific symptoms or concern

- Use tools
- Record your assessments and follow-up
- Do it regularly



Some examples..

- Brief Pain Inventory
- Spiritualy assessment − HOPE questions
- Bristol stool chart
- Hospital and Anxiety Depression Scale
- Kessler Psychological Distress Scale (K10)

It measures of psychological distrerss. It is not cancer/ transplant specific. Used by non specialist professionals (e.g. Gos, nurses) to refer patient to a psychological service.

K10 ASSESSMENT QUESTIONNAIRE

Date: _____ Patient ID Number: _____

For all the questions below please indicate the response which best describes your mood over the past 4 weeks.

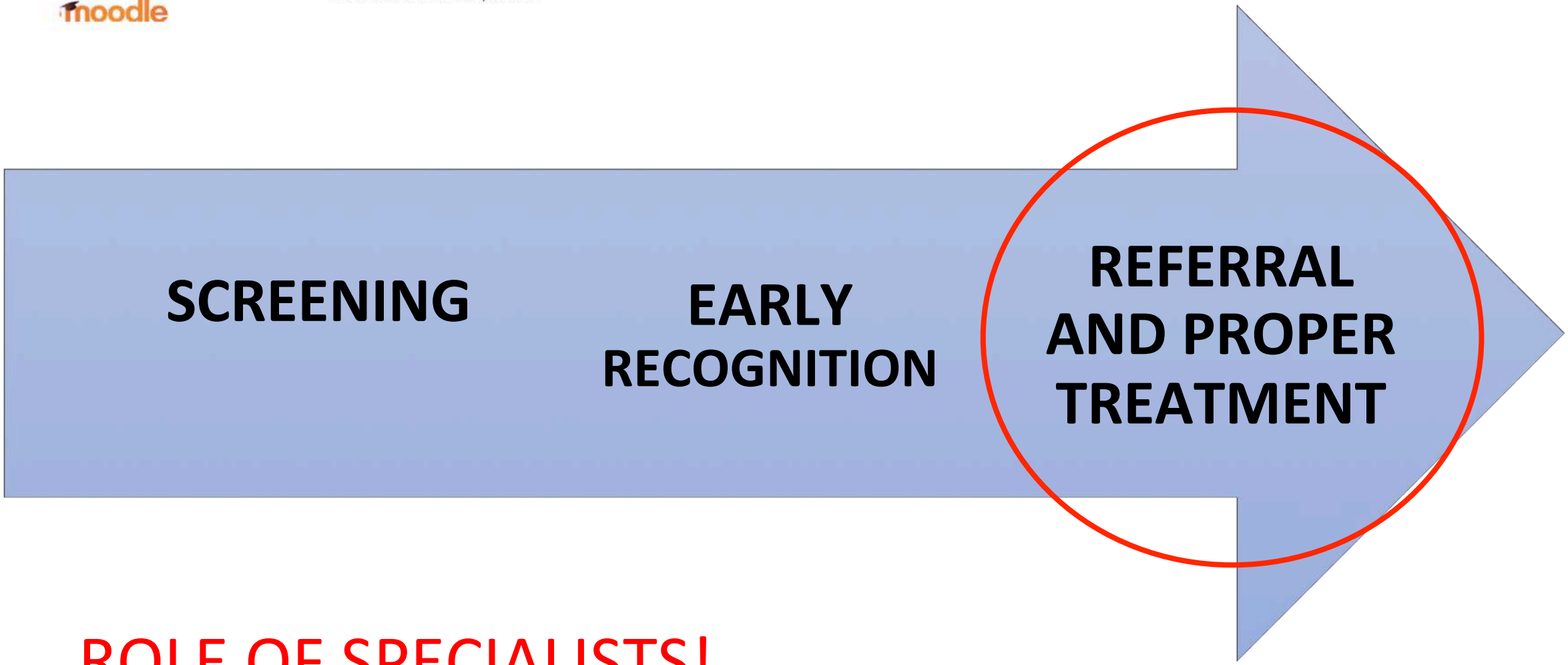
In the past 4 weeks	All of the time	Most of the time	Some of the time	A little of the time	None of the time
1 About how often did you feel tired out for no good reason?					
2 About how often did you feel nervous?					
3 About how often did you feel so nervous that nothing could calm you down?					
4 About how often did you feel hopeless?					
5 About how often did you feel restless or fidgety?					
6 About how often did you feel so restless you could not sit still?					
7 About how often did you feel depressed?					
8 About how often did you feel that everything is an effort?					
9 About how often did you feel so sad that nothing could cheer you up?					
10 About how often did you feel worthless?					

Ranges
< 16: no increased likelihood of anziety of depressive disorder

16-30: 3 times the population risk of having depression/anxiety

31-50: 10 times the population risk of having depression/anxiety

K1O assessment questionnaire



ROLE OF SPECIALISTS!

However, nurses are at the bedside during the all process of care

Qualitative studies state that…

Nurses….

- have an **active role** in **the recovery story** of HSCT patients
- contribute to the positive story
- support patients in their therapy
- act like **FACILITATORS** reinforcing and explaining concepts and information, especially when thing start going bad → patient reassurance and less panic
- give positive feedback

Coolbrandt, 2005

EXPERTISE → skills and knowledge to normalize concerns and complications. This increases the confidence and the trust relationship with patient and caregivers

Realistic hope vs hopeful realism

EMPATHIC ATTITUDE → understanding what the patient is going through, willingness to adjust the schedule if necesssary for the patient, and to pay attention to the person behind the patient

Early recognition and regular assessment are critical

WHEN TO MEASURE IT?

- Following diagnosis or status changes (recurrence?)
- Prior to each phase of treatment
- Follow-up
- Palliative care

- Document the screening/assessment results (Record!)
- Plan further assessment
- Evaluate the impact of unmet needs on daily living and Quality of Life.

SCREENING

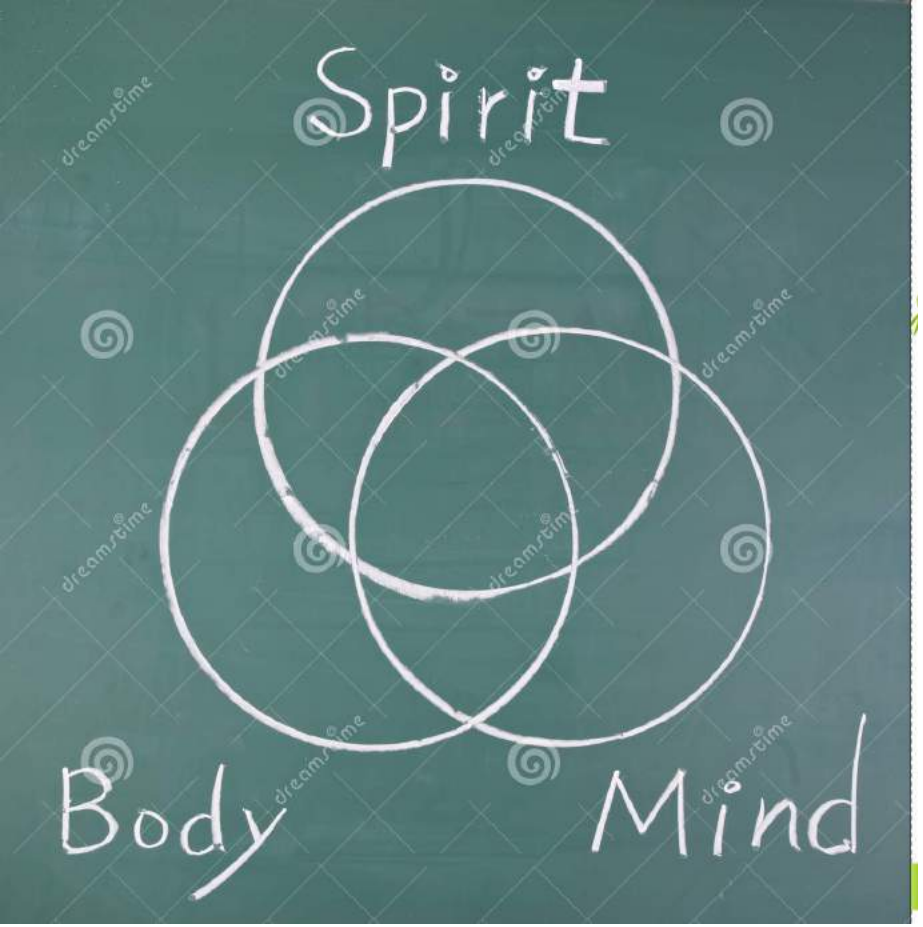
Identification of risk factors and possible unmet needs before it becomes problematic. This facilitate the immediate response to high-level risks.

Physical (I)

- Fatigue
- Pain
- Stiffness
- GI and bladder changes
- Cardiovascular and respiratory issues
- Sexual disfunction
- Fertility issues
- Weight changes
- Neurological symptoms
- Movement disfunction

Physical (II)

- Nausea
- Respiratory issues
- Balance
- Safety
- Falls prevention



PSYHOSOCIAL ISSUES can lead to a LOSS OF ENERGY

PATIENTS BECOME **DEPENDENT ON** THEIR CAREGIVERS AND PARTNER

PHYSICAL SYMPTOMS ENHANCE A SENSE OF DEPENDANCE (PAIN, FATIGUE..)

PATIENTS EXPERIENCE FEAR AND POWERLESSNESS FEELING A **LOSS OF CONTROL,** worsening with functional impairments and physical disfunction

Psychological

- Anxiety about the relapse
- Cognitive impairments
- Memory loss
- Fear
- Isolation
- Depression

TREATMENT? *YES WE CAN!*
..and we have to!

COGNITIVE BEHAVIOURAL THERALY

- Teaches skills in problem-solving, reframing attitudes, reinforcing coping strategies
- Relaxation therapy, guided imagery or cognitive skills

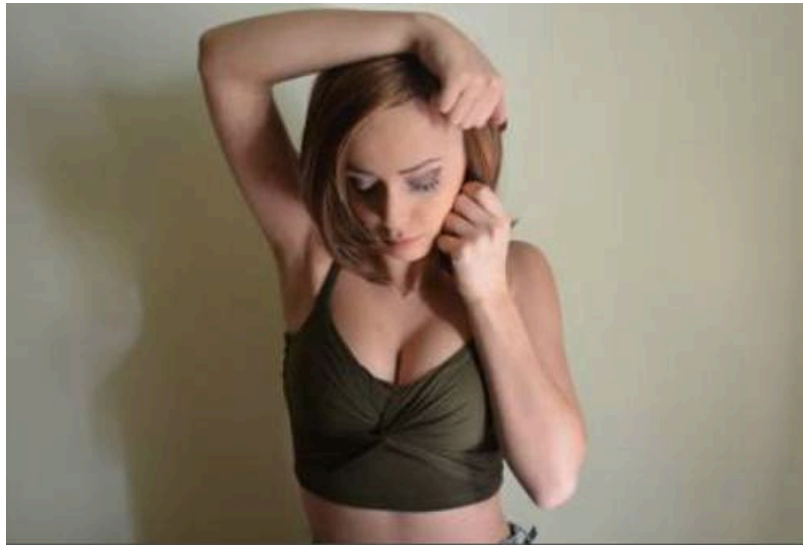
SUPPORTIVE PSYCHOTHERAPY

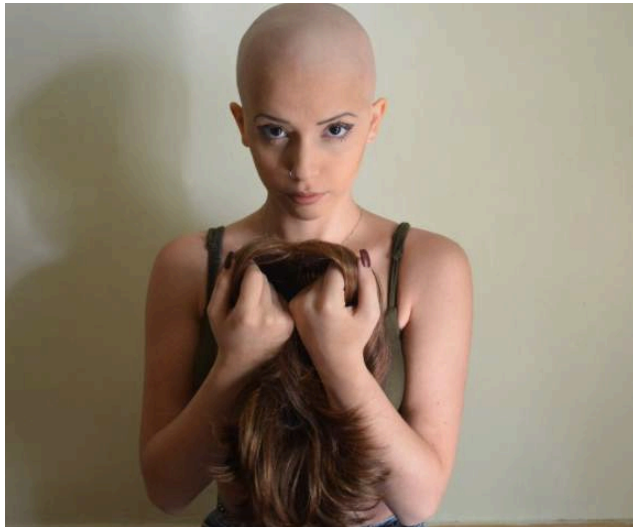
- Supports the expression of emotions. The individual experience has an enormous value. Reinforce the strenghts of the inividual and strenghten coping techniques.

- **GROUP OR FAMILY GROUP/COUPLE THERAPY**

Focus: sharing of experiences among patients with similar clinical stati and experiences. Patients feel they can help somebody with theire expeirence.

It improves mood, coping techniques, adjustment, anxiety and depression. Positive immune function changes.





BODY IMAGE AND BODY CHANGES

These can cause dysfunction and low self-esteem.

Patients may feel uncomfortable with their new physical appearance, even if temporary.

Take care of adolescents : they confirm themselves through their body and their appearance.

Information

CONSIDER THAT INFORMATION IS

A PATIENT RIGHT and a NEED.

DO NOT FORGET CAREGIVERS AND FAMILIES.

- Treatment benefits
- Management of side effects of treatment
- Follow up care
- Advanced care planning
- Care needs

Find strategies and involve the patient! Self-care and empowerment.

CONSIDER THE UNICITY OF THE INDIVIDUAL AND THE PERSONAL NEEDS OF SPECIFIC INFORMATION, IN THE PROPER WAY.

Verbal advice?

Written information?

In person meeting?

Contact details for a service or a support group?

- Patient **preferences for communication** styles vary: health care professionals need to tailor the format of information provision
- Information recall must simplify the language: suggest the KEY ISSUES and the KEY MESSAGES.
- Provide PROPER TIME in a PROPER PLACE (privacy!!)
- Respect individual preferences for the amount, detail and content of information.
- Promote questions (e.g. question sheet: reduction of anxiety and expectations)
- Provide good resources (written, online, audio-video) to reinforce information and support the individual understanding.

FIGHT THE SENSE OF LONELINESS

Support the **social network** around the patient: family, friends, group of patients, health care staff.

Do not forget that, due to the disease, patient could have **changed his/her role** within a group → sense of sadness, powerlessness, frustration.

Consider the presence of **a trusted person** who could take part to the information process and be involved in the decision-making process.

OFTEN, THERE IS NO IMMEDIATE SOLUTION FOR PROBLEMS.

PATIENTS HAVE TO GO THROUGH THE SITUATION.

Check list to **appraise interactions** with patients and families

- Introduce yourself to the person and their family, and ensure a comfortable environment, minimise interruptions.
- Assess the anxiety levels of the person and their family, normalise feelings of anxiety. If the person has a history of anxiety disorders such as needle phobia, refer the person to a psychologist for extra support.
- Provide an overview of the session, the structure, timeframe and ensure you allow time for questions.
- Assess understanding and correct any misconceptions.
- Assess level of information required.
- Teach relevant concepts e.g. introduce and discuss the treatment.
- Introduce concept of self-care.
- Review who to contact and role play how and when to make contact.
- Provide information in multimedia format, use diagrams or pictures where possible.
- Encourage the presence of another person.
- Ask the person to repeat back to you their understanding of the information you have provided.
- Repeat the important information in a follow up session / phone call. Send a summary letter as a follow up to the information.

Health care staff must promote STRATEGIES to meet specific supportive care needs

FIRST, SELF-MANAGEMENT SKILLS.

It is essential that staff encourages patient awareness and active partecipation of the indicivual to minimise the consequences of treatment, promote survival, health and well-being..

PARTNERSHIP between the person and the staff.

- **PATIENT AS THE BEST SOURCE OF INFORMATION ABOUT HIS CONCERNS, HIS FEELINGS**
- CONSIDER THE PERSONAL MEANING OF HEALTHY LIFE, NORMAL LIFE AND PRIORITIES
- PROMOTE INTERDISCIPLINARY WORKING
- EVERYBODY INVOLVED IN THE PROCESS OF CARE HAS TO BE AWARE OF THE DIVERSE RESOURCES AVAILABLE AND HOW AND WHEN PROMOTE THEM

Trust the Patient

Consider patient awareness and capability to take care of him/ herself: which kind of resources does the patient have?

- Facilitator
- Adapt the rules
- Be flexible

Assess	Advise	Agree	Assist	Arrange
Beliefs and knowledge of the person	Specific information to correct myths. Tailored provision of information.	Shared decision making: identification of goals and priorities, pathway of care with patient	Identification of barriers. Find strategies to overcome them.	Follow-up call, review achivement of set goals

Patients do not want their caregivers and relatives to wear their burden.

They need their presence, feeling **that they are nearby.**

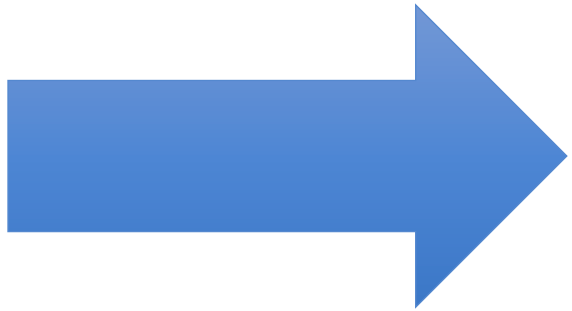
Thus, they can be **indipendent** and decide how to COPE with the situation.

PRESENCE IS AN INTERVENTION ITSELF

The importance of the referral for specialised services and programs

….dedicated to?

- Financial risk
- Cultural and linguistical diverse background
- Patients experiencing hopelessness, persistent physical symptoms, pre-morbid mental health issues.



REFERRAL SHOULD BE EVIDENCE BASED AND CONTEXTUALIZED.
IT IS SUGGESTED THAT SERVICES ESTABILISH REFERRAL NETWORKS AND HAVE A CONTACT LIST OF LOCAL SERVICES AND RESOURCES.

Patient needs to consent to the referral

Prioritise referrals (exacerbations of symptoms)

Multidisciplinary team and approach: standard approach to care

Normalise the need for referral to other discipline

Coordinate the program (Care manager?)

Consider the timing of the referral. Do not forget that it is better early than late, and prevention than treatment.

Suggest referral at an appropriate time.

Barriers to psychological care

PATIENT REASONS

- Fearing stigma
- Fearing being a burden on busy clinical staff
- Fearing distracting the physician from curative efforts
- Thinking that distress is inevitable

STAFF REASONS

- Time constraints/ competing medical issues
- Discomfort with or disinterest in psychosocial issues
- Uncertainty about the value of psychosocial intervention
- Lack of training and lack of institutional support

Care about the provider!

RISK OF STRESS OR COMPASSION FATIGUE

- accumulated losses
- Emotionally charged care
- Sustained and exclusive focus on severe conditions, several complications, terminal illnesses and care
- Mortality issues of the cliniciand

Care about the provider! (II)

- Examine your own thoughts, feelings and attitudes regarding death and dying −> find coping strategies
- Peer support (especially in novice nurses)
- Talk about death and death communication → you will become more comfortable and confident while talking with patients and families

If nurses and staff do not manage their own distress and needs..

- Higher risk of medical errors
- Increased turn-over and absenteeism
- Reduced quality of care
- Reduced satisfaction expressed by recipients of care
- Higher risk of burnout and affection of personal life

In order to provide better care, improve the patient quality of life and quality of care, due to the nature of HSCT treatment and patient conditions, **EARLY PALLIATIVE CARE** should be integrated with transplant and oncology care.

Palliative care is a multidisciplinary approach to symptom management, psychosocial support and assistance in treatment decision-making for patients with serious illness and families. It emphasizes well-being at any point along the disease trajectory.

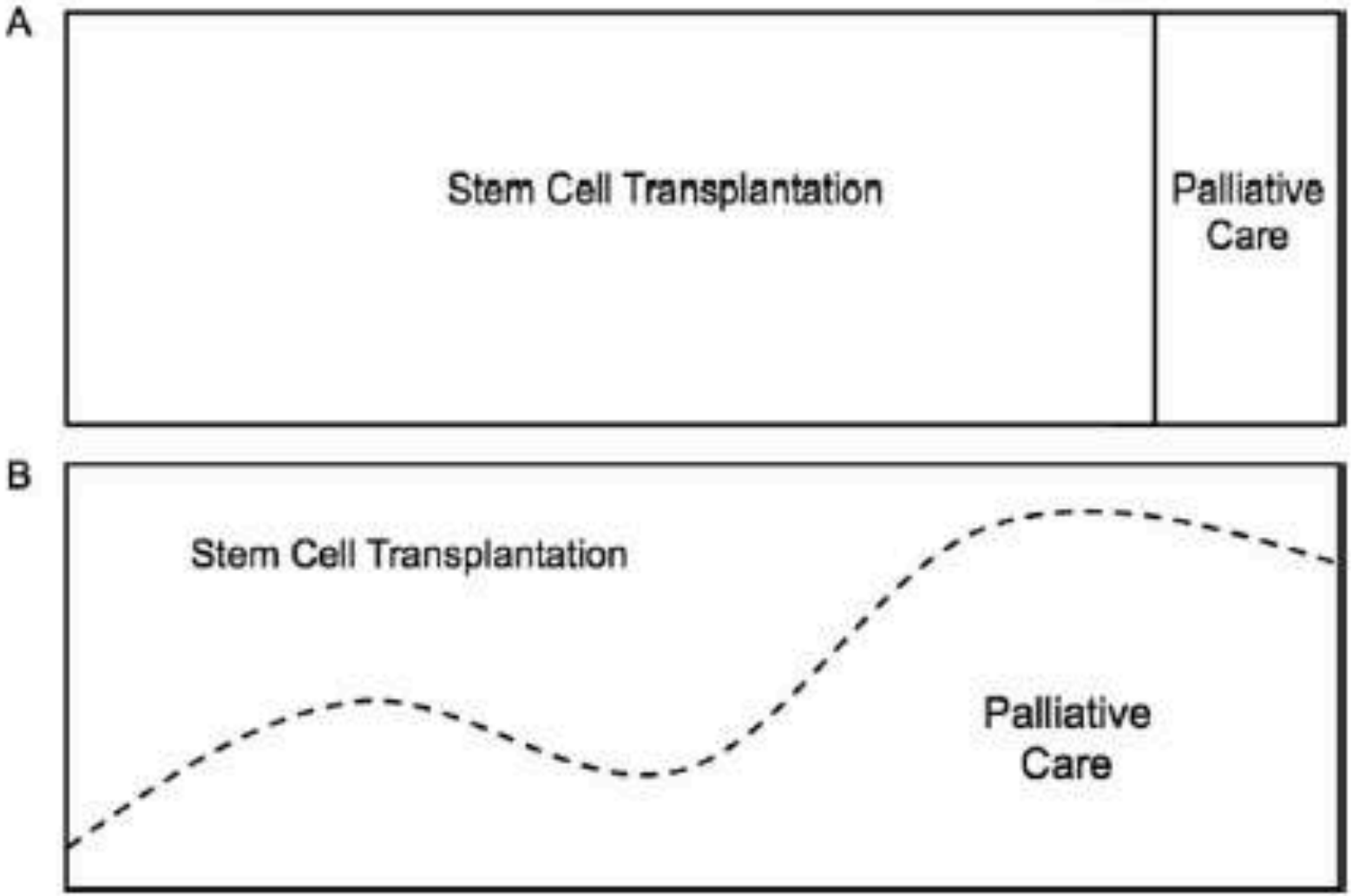


Figure 1. The continuum of care in stem cell transplantation. (A) "All or none" approach. (B) Early, simultaneous PC integration into SCT standard of care.

Hematology, 2015

Why are palliative care different?

1) More experience and more tools for complex symptom management
2) Expertise in helping patients cope and adapt to their illness and manage their EXPECTATIONS during transplant process
3) Maximization of quality of life during and after disease treatment

Lack of integration and rare use of palliative care services. Why?

- HSCT is an intensive therapy aiming to cure the disease → different goals
- Difficulty to clarly define the transition between curative phase and palliative phase of treatment → delay
- Blood cancers are often associated with rapid and unpredictable trajectory of decline at the end of life
- Staff misperceptions, mistrust, lack of knowledge about palliative care

Table 1. The canyon: challenging misperceptions of each other

PC misperceptions of SCT	SCT misperceptions of PC
Disease is the enemy	Suffering is the enemy
Death is failing	A "bad death" is failing
Protocol driven	Empirically driven
All science and data	No good science
Ignore suffering	Ignore cure
SCT means torture	PC means giving up
Do not communicate with patients	All talk and no action
Do not inform patients of risks	Talk patients out of life-saving treatments

Strategies to promote integration

BREAKING MISPERCEPTIONS ABOUT PALLIATIVE CARE

The focus is on addressing physical and psychological symptom burden in patients undergoing HSCT with curative intent → correct misperceptions about appropriate timing for palliative care. Build a trust between palliative care and HSCT team

CREATE A COLLABORATIVE ENVIRONMENT BY ENGAGING PALLIATIVE CARE TEAM

Plan and discuss integrated care model and workflow. Discuss strategies and barriers.

BILATERAL LEARNING EXPERIENCE

Both teams have specific expertise. They can learn one from another, enhancing patient care and outcomes.

CONSIDER THE SIMILARITIES

-individualized care, patient-centered

-emotionally involving patients

-multidisciplinary team

A multidisciplinary palliative care team **help manage the primary** LATE EFFECTS for CANCER SURVIVORS including FATIGUE, DEPRESSIVE SYMPTOMS, ANXIETY, DISTRESS, PAIN, SLEEP DISTURBANCE.

GOAL
Patient and family COMFORT

Primary Goal
consider the individual priorities and values of patients through specialized, interdisciplinary care and communication

Palliative care can relieve symptoms and treat patients'emotions, by teaching coping skills and helping managing fear and anxiety.

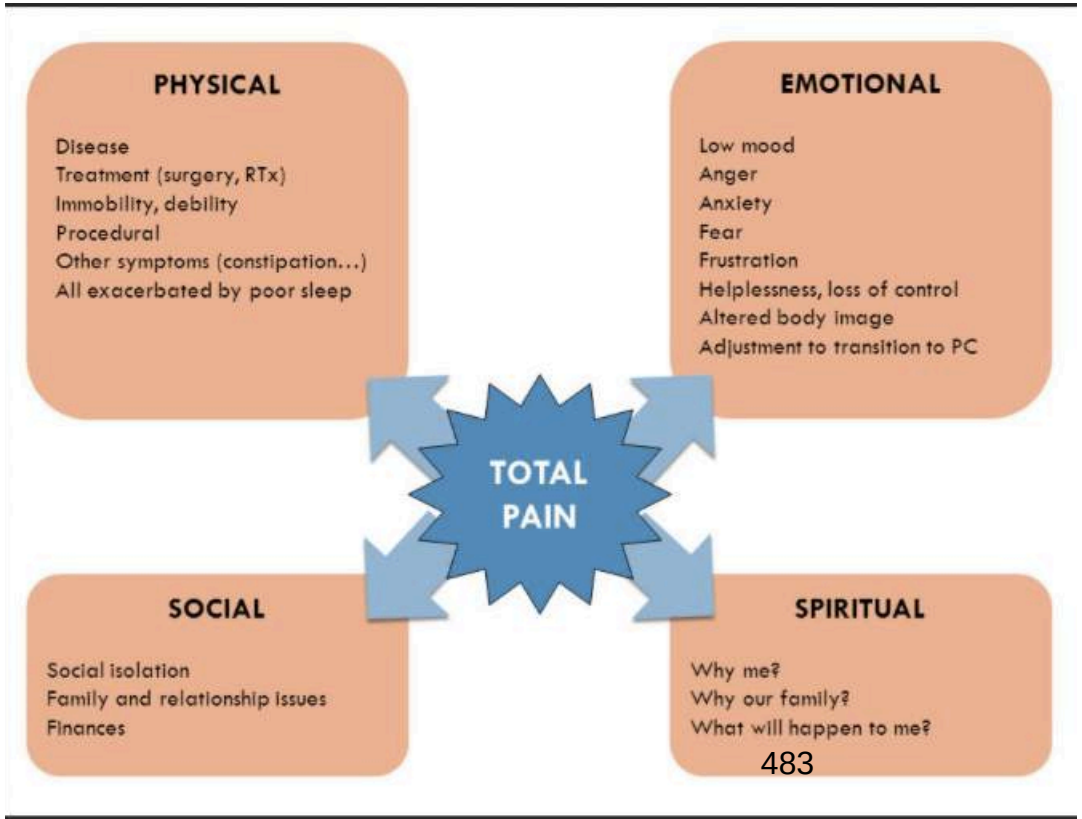
PHYSICAL SYMPTOMS

PSHYCOSOCIAL BURDEN

PAIN

Pain Management: principles

- Pain is often under-treated
- It cannot be considered in isolation. It is a part of a multidisciplinary approach → TOTAL PAIN



- Make patients and families aware of benefits of opioids. Let them understand that respiratory depression and the development of tolerance/addiction are not problems if drugs are used properly

Opioids severe side effects are AVOIDABLE!

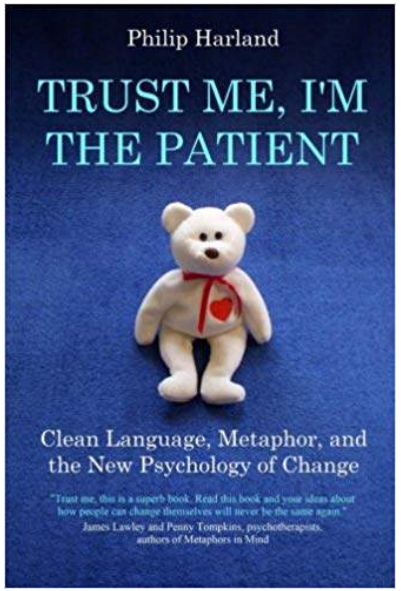
Pain control is achieved in most palliative care patients but 10 – 20% of them mantain discomfort and uncontrolled pain.

Difficult control of pain

- Neuropathic
- Incident
- Multiple
- Opioid resistant
- Side effects to analgesics
- Total body pain
- Fear of analgesics

TRUST THE PATIENT

- Assess, identify, treat, assess the pain
- Evaluate pain regularly, using proper tools
- Prevent pain and reduce accompayning symptoms that could cause discomfort
- Anticipate side effects



4 step approach to the use of analgesics in the Palliative Care setting

REDUCE THE NOXIOUS STIMULUS

History and physical examination: identify the stimulus

Investigation ONLY if needed. Do not influence PATIENT COMFORT

Give regular Paracetamol or consider non steroidal antinflammatory drugs or steroids (if an inflammatory process is ongoing)

4 step approach to the use of analgesics in the Palliative Care setting

RAISE THE PAIN TRESHOLD

Identify issues that are exacerbating pain

Consider Sleep, Anxiety and Depression (consider also pharmacological intervention)

4 step approach to the use of analgesics in the Palliative Care setting

CONSIDER OPIOIDS

Early use of opioids, especially for moderate or severe pain

4 step approach to the use of analgesics in the Palliative Care setting

CONSIDER ADJUVANT ANALGESIC

If the pain does not respond to the opioids administration.

Common adjuvants are:

- Steroids
- Anticonvulsivant
- Antidepressant
- NMDA guidelines

Supportive Care of HSCT

Nutritional Support

Background & Introduction

HSCT as a highly stressful condition requiring a **high level of energy**

HYPERMETABOLIC STATE

>> catabolism and anabolism

Up to 1 y after HSCT **in 50% of patients**

Conditioning regimen

GVHD

Infections

Organ failure

Tissue repairing

Prolonged vomiting

Diarrhoea

Appetite reduction

Intestinal obstruction

Mucositis

Psycho-emotional factors such as ansiety, depression, fatigue, can be contributing factors

Within few days of admission to hospital:

- **Reduction of calorie intake**
- **Decrease in body weight**

Impaired nutritional status before HSCT is a **negative prognostic factor** for outcome after transplant

Better nourished patients have a shorter time to engraftment

- lower risk of infection

- **shorter hospital stays**

- **lower costs**

Higher TRM has been observed in underweight patients (BMI $\leq$20)

Goals of nutritional support?

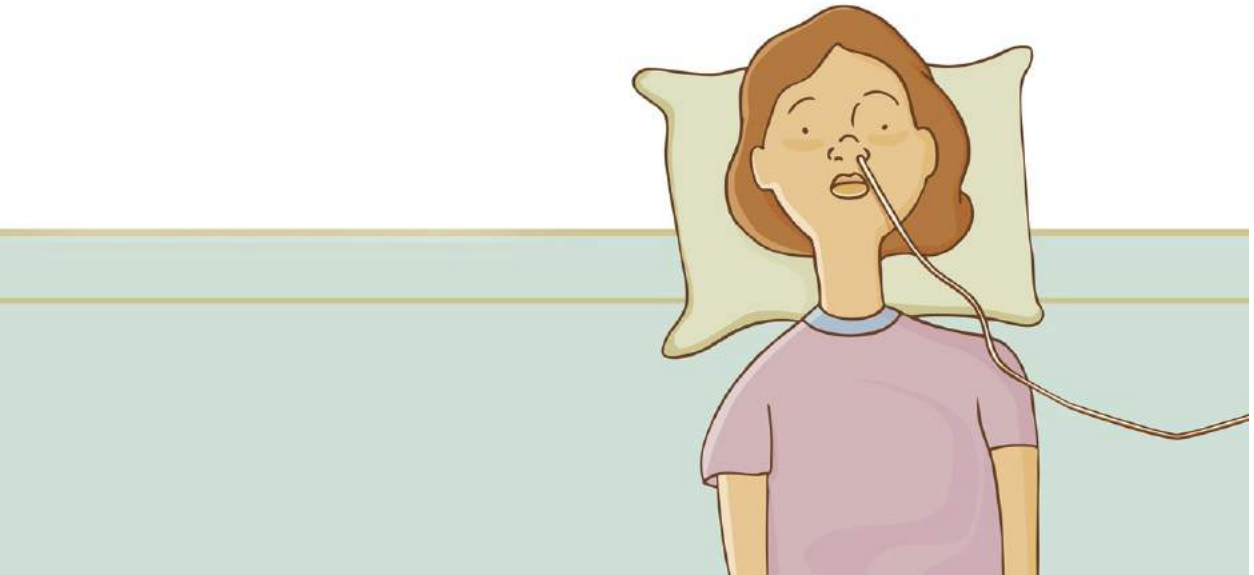
- Prevent loss of weight, body mass, fluid and electrolyte imbalance
- Improve patient health outcomes and prevent/reduce complications
- Increase patient comfort

Optimum delivery *of nutrition support becomes essential* ***early*** *on in the course of treatment for a BMT*

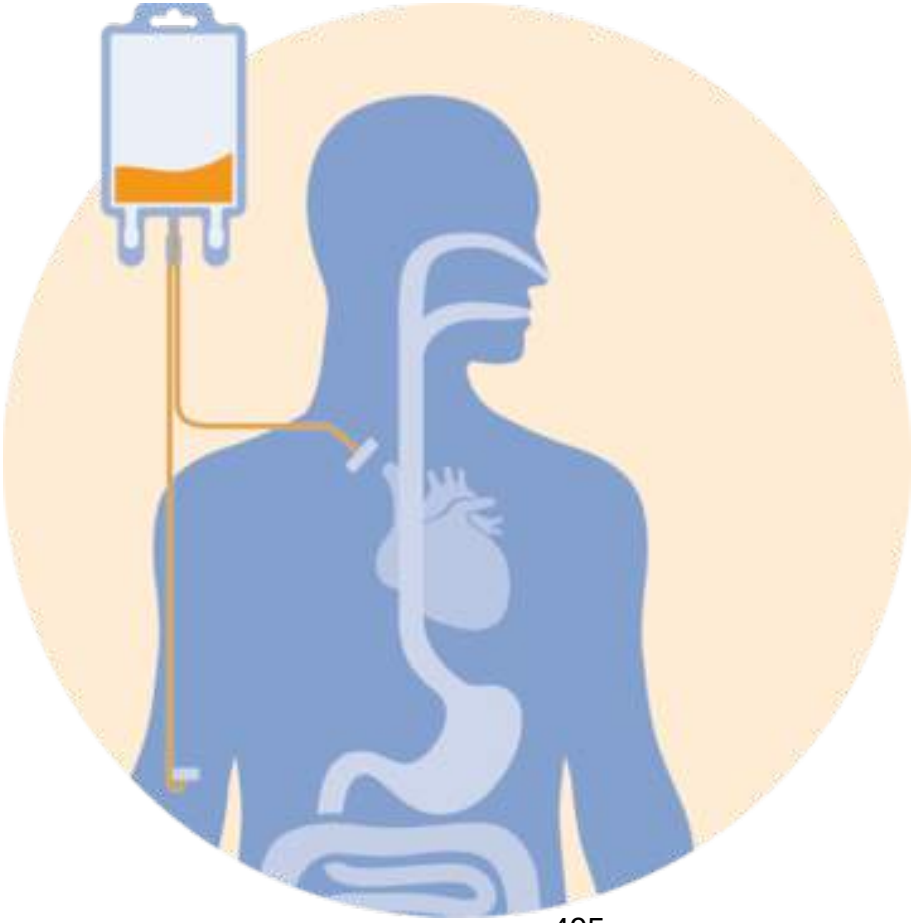
Key points : how and when

- Oral Nutritional Supplements
- Intravenous administration of nutrients

Enteral Nutrition



(total) Parenteral Nutrition



Write down

one GOOD aspect and one BAD effect

of EN and PN

Evidenced based practice & Indications

Total Parenteral Nutrition (TPN or PN)

- severe mucositis or severe radiation enteritis
- Intractable vomiting
- Intense diarrhea

Complications
- Metabolic
- CVC related (infections)

Evidenced based practice & Indications (II)

Enteral Nutrition

- Mantainance of the intestinal trophism
- Faster way back to oral route
- Mucositis: grade I or II (WHO scale)

- Risk of bleeding and GI tract ulceration
- Patient compliance (children!) and tolerance

Evidenced based practice & Indications (III)

TIMING IS CRITICAL

Use the nutritional artificial support only when needed!

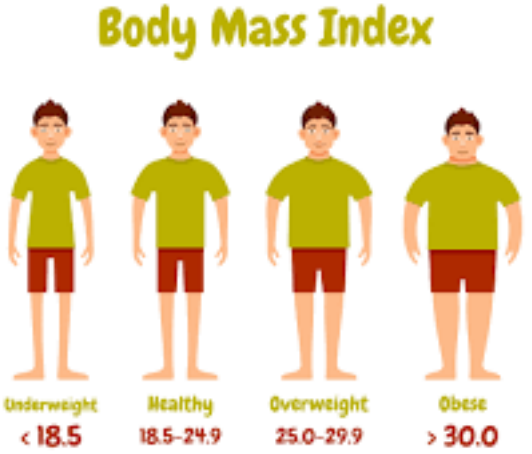
- Routinely early administration of TPN before conditioning regimen?
- Early inserction of NG tube if severe mucosa complications are expected?

- TPN should be progressively decreased while the patient can cover > 50% of the daily energy requirements orally
- Not administer TPN routinely in autologous recipients (consider the mucositis severity)

- If no clinical controindications, patient should come back to oral route as soon as possible

Nutritional Status Assessment

- **BMI**
- **Nitrogen Balance**
- Laboratory test
- Patient preferences and habits



Nitrogen Balance should be considered the most accurate way to perform nutritional assessment in BMT patients.

Screening and early identification of risks

Timing

Tools: MUST – Malnutrition Universal Screening Tool / MNA – Mini Nutritional Assessment

Patient and caregivers information and education

Body Mass Index (BMI)

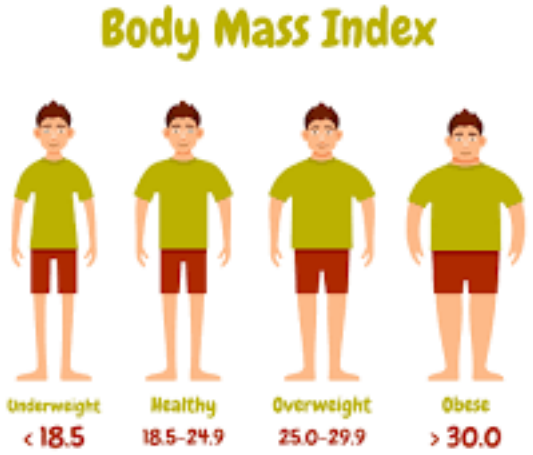
Measure of body fat based on height and weight that applies to adult med and women

Discussion

Nutritional support as a **process**

(Botti et al. 2015)

Screening and formal assessment of nutritional status



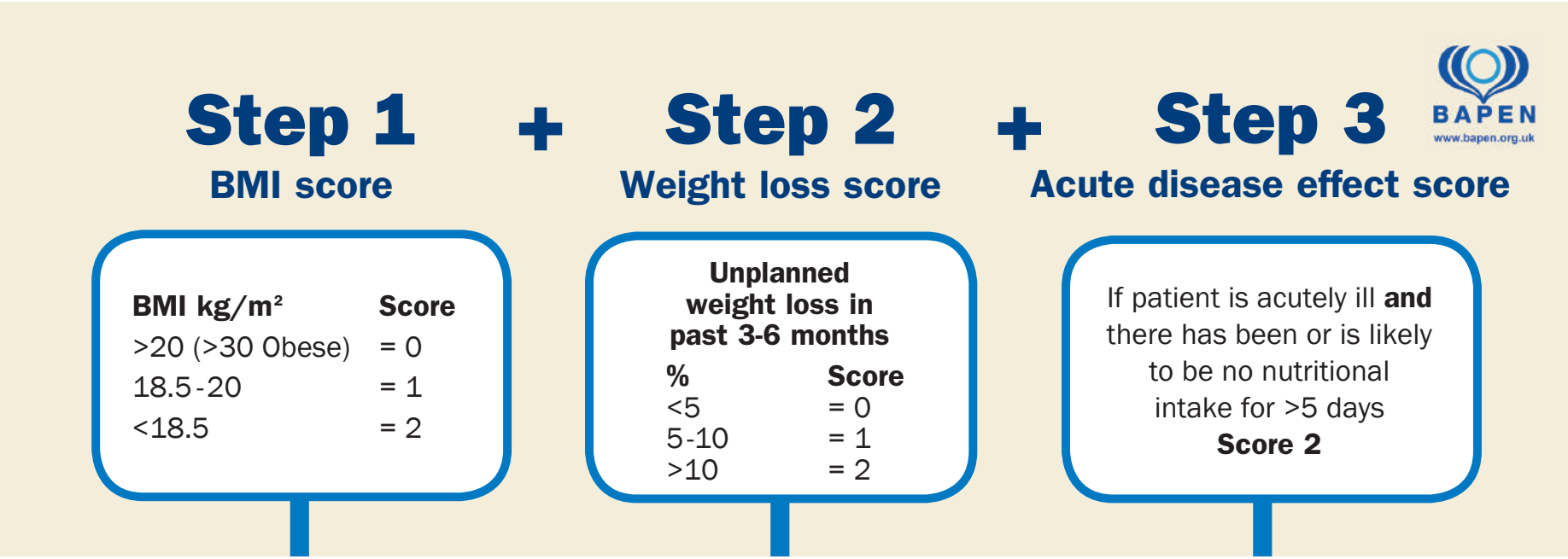
- **BMI**
- **Nitrogen Balance**
- Laboratory test
- Patient preferences and habits

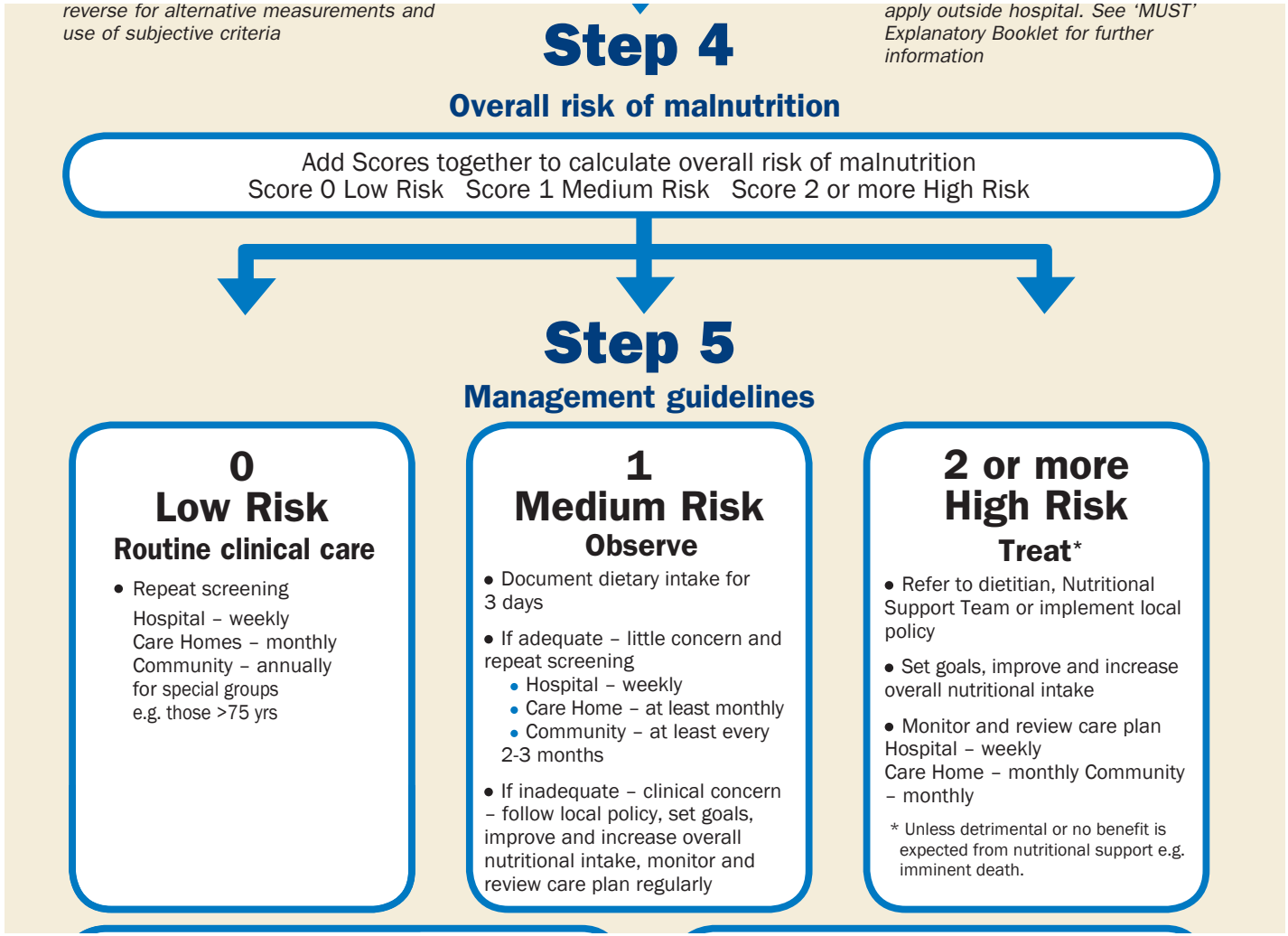
Nitrogen Balance should be considered the most accurate way to perform nutritional assessment in BMT patients.

TIMING – FREQUENT RE EVALUATION – FOLLOW UP - **TOOLS**

It is a “MUST” to measure it!

Malnutrition Universal Screening Tool





Identification of risk

Management

www.bapen.org.uk

Discussion (II)

WHAT'S NEXT?

- More trials needed (timing, association of nutritional supports, best nutritional assessment)
- Local institution procedures to define nutritional screening, follow-up, roles and rules within the..
- Multidisciplinary team and integrated care (MD, RN, dieticians, physical therapist)
- Patient and caregiver empowerment: parthership

Conclusion

- Nutritional support is imperative to prevent malnutrition and poorer outcomes
- Nutritional status has to be closely monitored to early identify malnutrition
- Choose the best way of deliver nutritional support: way of administration, timing and device
- Increase patient comfort and compliance
- Evidence Based Nursing Practice: device management, prevention of infections, proper administration of nutritional support
- Follow- up patient after discharge: assessment and educational program for patients and caregivers

Literature reference

- *Murray SM, Pindoria S (2017) Nutrition support for bone marrow transplant patients (Cochrane Review)*
- *Hadjibabaie M et al (2008) Evaluation of nutritional status in patients undergoing HSCT (BMT 24, 469 – 473)*
- *Wilson S et al (2014) Parenteral nutrition utilization in Bone Marrow Transplant Recipients (Journal of Nutrition and Health Sciences 1,1)*
- *Rzepecki P rt al (2010) Blood and marrow transplantation and nutritional support (Support Care Cancer, 18: S57-65)*
- *Ferreira et al (2014) Nutritional status of patients submitted ti transplantation of allogeneic HSC: a retrospective study (Rev Bras Hematol Hemoter. 36 (6): 414-419)*
- *Botti S et al (2015) Nutritional support in patients undergoing HSCT: a multicentre survey of the GITMO transplant programmes (Ecancer, 9:545)*
- *Browning B et al (2006) Weight loss and reduced body mass index: a critical issue in children with multiorgan cGVHD (BMT, 37; 527 - 533)*
- *Jim et al (2012) Supportive care of HSCT patients (Biol Blood Marrow Transplant, 18: S12-S18)*
- *El – Jawahri et al (2016) Effect of inpatient palliative care on quality of life 2 weeks after HSCT: a randomized clinical trial (JAMA, 316 (20): 2094:2103)*

Literature reference

- *Roeland E (2015) Spanning the canyon between stem cell transplantation and palliative care (Hematology 2015)*
- *LeBlanc TW (2015) When and why should patients with hematologic malignancies see a palliative care specialist? (Helatology Am Soc Hematol Educ Program, 2015: 471,7)*
- *Masel EK et al (2018) Demystification od palliative care: what palliative care teams don't want you to think about them*

Going Home After Bone Marrow Transplant

Sherin P Babu
Incharge
Haematology Nursing and BMT unit
RGCI&RC Delhi

Rajiv Gandhi Cancer Institute and Research Centre

Introduction- Thinking about going home

Preparation of home

- Keep your home as free of dirt and dust as possible
- Do not try vacuuming and dusting of the rooms, clean with mopes atleast once
- You shouldn't be around any renovations or construction
- Bathroom should be cleaned with disinfectants regularly
- You can use an air filtration system in your home, but it isn't necessary.

Pets ; Can carry diseases –greater risk of infection while on recovery period ; avoid close physical contact

Family and visitors ;

- Can have close physical contact with those in your immediate family.
- Wear a mask if you must be in the same room with someone who's sick or you have many visitors
- You can have visitors, but limit them to small groups
- Avoid people who are exposed to cold, cough or any bacterial /viral infections recently

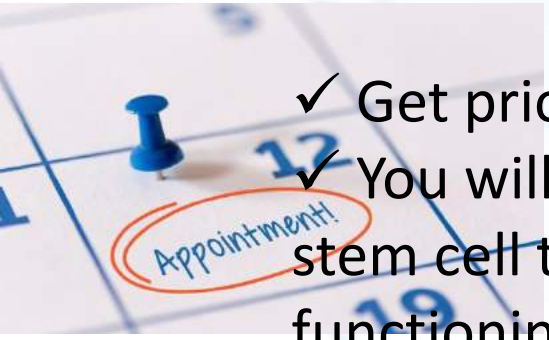
Medications

- Immuno suppressants

Other prophylaxis

- Acyclovir
- Sulfamethoxazole and Trimethoprim
- Avoid aspirin and NSAIDS
- Don't take any herbal supplements or home remedies without talking to your transplant team
- If transfusion required – use Irradiated blood products

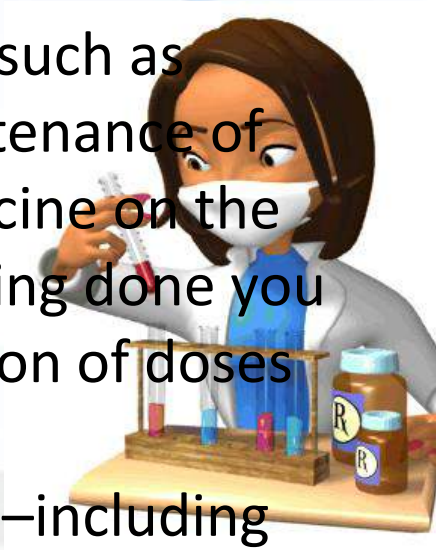
Follow Up Instructions



✓ Get prior appointment for the scheduled revisit.

✓ You will have frequent checkups and tests after your stem cell transplant until the new bone marrow is functioning properly.

✓ If you are taking any immunosuppressant's such as Tacrolimus or Cyclosporine which needs maintenance of the therapeutic levels– do not take such medicine on the day of the revisit , carry it and once the sampling done you can have it. Ask your doctor for any modification of doses before the next dose .



✓Carry all the necessary documents with you –including discharge summary, reports etc

Care of CVAD's

- As much as possible, use the arm with the PICC in it for normal daily activities. Lack of movement can lead to blood clots
- Avoid activities or exercises that require major use of your arm, such as sports
- Avoid lowering your chest below your waist-When your chest is below your waist for a long time, the catheter's internal tip could slip out of place in the vein
- Don't use any sharp or pointy objects around the catheter and don't let anything pull or rub on the catheter
- Periodical dressing and flushing of lines -Keep the dressing clean, dry, and secured to the skin. If it gets wet or torn, change it
- Avoid wetting – use waterproof cover to protect it from getting wet.
- Avoid weight lifting
- Report Leaking or damage, development of redness or warmth in the insertion site, pain, swelling in the arm etc

When to notify your Doctor?

- Related to GVHD
- Related to infections
- Related to relapse
- Non specific

Related to GVHD

- Skin: redness, rash , dryness, itching, tightness, or thickening o
- Digestive tract: decreased appetite, difficulty swallowing, nausea and vomiting, frequent watery diarrhea, greenish or bloody diarrhea, abdominal cramping, or weight loss.
- Eyes: dryness, irritation, burning, itching, sensitivity to light.
- Mouth: dryness, redness, white patches, sores, taste changes.
- Lungs: difficulty breathing, being short of breath, less able to exercise, worsening fatigue.
- Vagina: dryness, burning, itching, frequent infections, pain during sex.
- Joints: tenderness, stiffness, tightness.

Related to infections

- Fever of 100 degree or higher
- Chills, shivers, rigors
- Very low body temperature
- Rapid pulse
- Rapid breathing
- Burning/pain in urination
- Nasal congestion
- New onset of pain /cough
- Diarrhoea,vomiting ,pain abdomen
- Sore throat/ new mouth sores

Related to Relapse

- A pale complexion from anemia, Bone and joint pain.
- Bruising or petechiae /Prolonged bleeding from minor cuts
- Swollen gums
- Loss of appetite and weight loss
- Shortness of breath during normal physical activities
- Fever and Recurrent infections.
- Abdominal pain, Swollen lymph nodes.
- Dyspnoea , or difficulty breathing.

Non-Specific

- CMV infections
- Non-infectious pulmonary complications

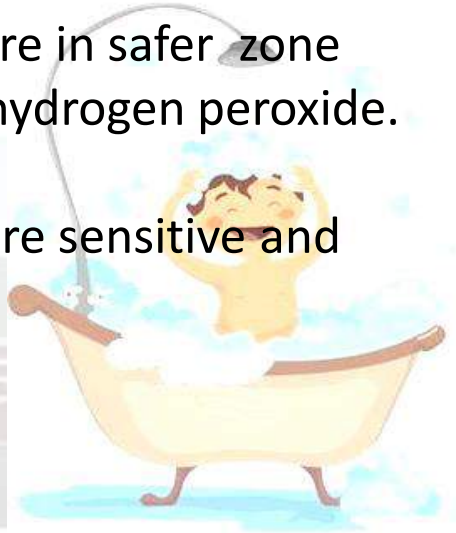
Includes pulmonary oedema, Upper airway complications, Diffuse alveolar hemorrhage, Cytolytic thrombi, and pleural effusion. Bronchiolitis obliterans, Veno-occlusive disease

- Secondary malignancies
- Organ toxicity

Pay close attention to hygiene

- ❑Take a shower or bath every day using mild soap
- ❑For dry skin use baby oil /mild skin lotion during or after your shower or bath.
- ❑Do not share towels or facecloths with other family members. Use clean dress.
- ❑Use an electric razor for shaving. Do not shave with a regular razor until your platelet count is 50,000 or more and you do not need any platelet transfusions.
- ❑Mouth care-Use ultra soft brushes till your platelets are in safer zone Don't use commercial, alcohol-based mouthwashes or hydrogen peroxide.

- ❑Limit your time in direct sunlight. Your skin will be more sensitive and may burn more easily after your transplant



Infection prevention

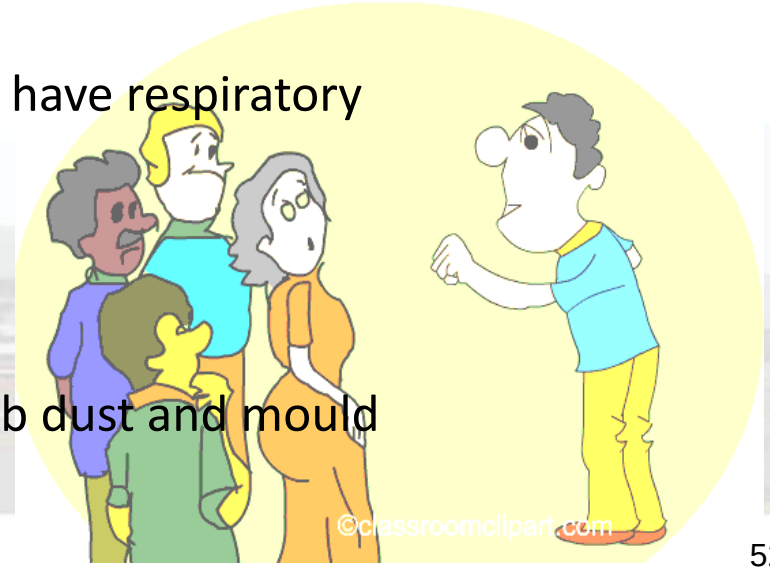
Prevent infections by direct contact

Hand washing is necessary:

1. Before eating/ before and after preparing food
2. After touching pets or animals
3. After sneezing ,coughing or blowing your nose
4. After going outdoors
5. Before taking oral medicines
6. After touching soiled linens or clothes
7. Can use alcohol-based hand sanitizer.

Prevention of respiratory infections

- Avoid close contact with people who have respiratory illness
- Avoid crowded areas.
- Avoid construction sites.
- Avoid tobacco use
- Avoid house cleaning that will disturb dust and mould
- Use face masks



Diet and fluids

- Can have boiled cooked food items, Avoid reheating
- Thick skinned fruits
- Cooled boiled water/ mineral water
- Foods to avoid:
- Raw or uncooked meat, poultry and sea foods.
- Raw or uncooked eggs
- Unpasteurized dairy products.
- Unwashed /raw fruits/vegetables
- Avoid fast foods

Personal relationships

❑Sexual relations : After a transplant its very normal to have concerns about intimate relationship and sex. Its safe to resume sexual intercourse once your WBC count and platelets are in safer zone

❑ Use Birth control measures to avoid pregnancy.

'Life after Bone Marrow Transplant is a transition Period between "Home Coming" to leading a life which is "new normal."

Cell source and Apheresis

Aleksandra Babic
BMT Unit Coordinator and QM - Oncology Institute of Southern Switzerland, IOSI – Bellinzona, CH

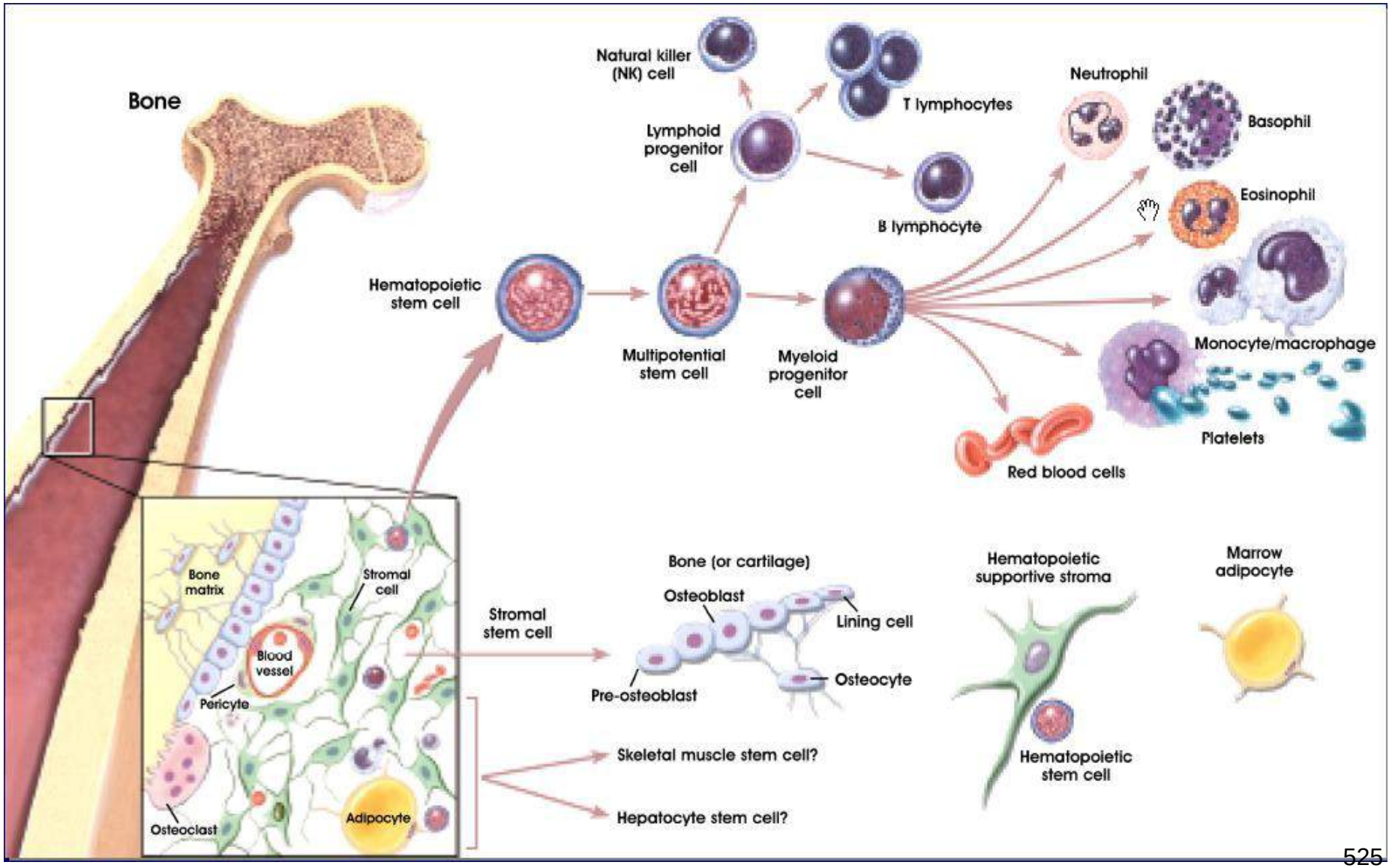
Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

Learning objectives

- HSC source, standard and new applications
- Administration of growth factors for HPC mobilization and for post transplant hematopoietic cell reconstruction
- HPC processing: principle of HSC collection procedures
- HPC cryiopreservation
- ECP for GvHD

Hematopoietic stem cells



APBSC Transplant Process

1 Injection of mobilising agents

2 Mobilisation

3 Collection

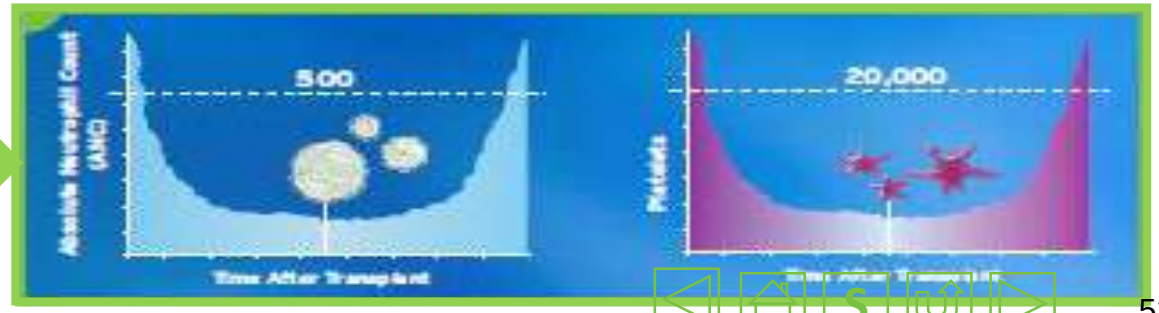
4 Preparation & storage

5 Cryopreservation

6 Chemo / radiotherapy

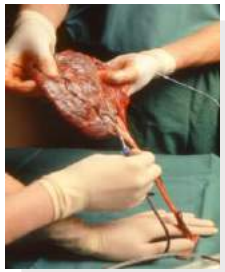
7 Stem cell transplant

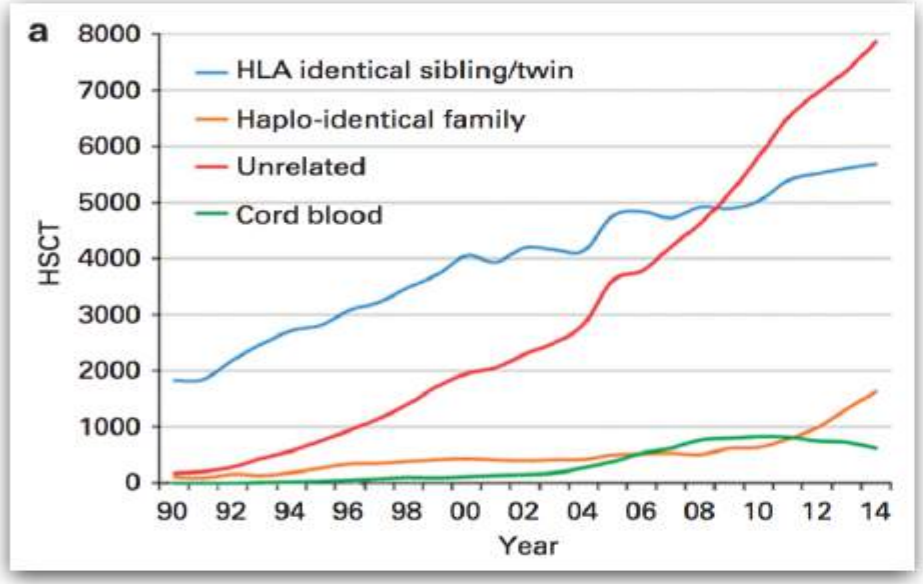
8 Engraftment & recovery

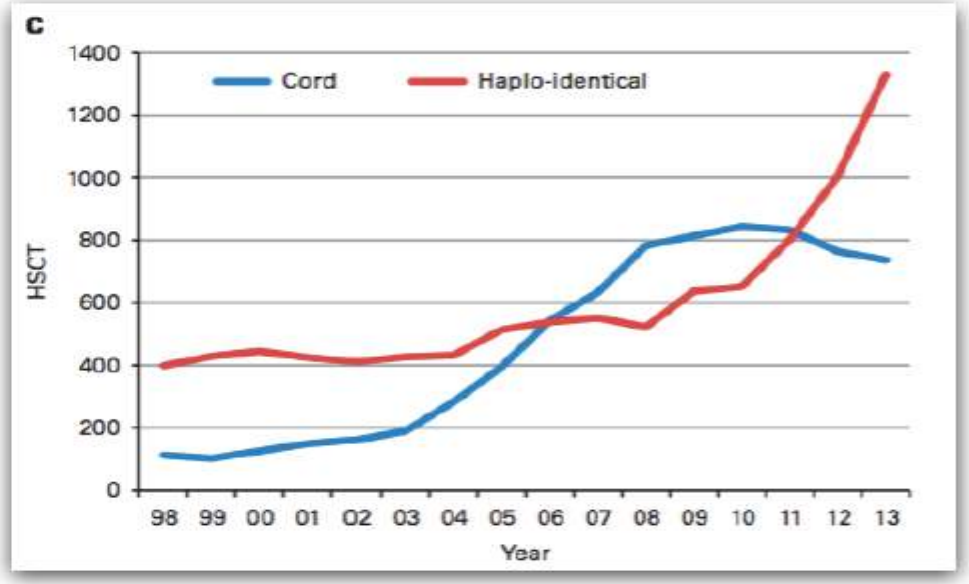


Cell source

- Bone marrow
- PBSC
- Cord blood

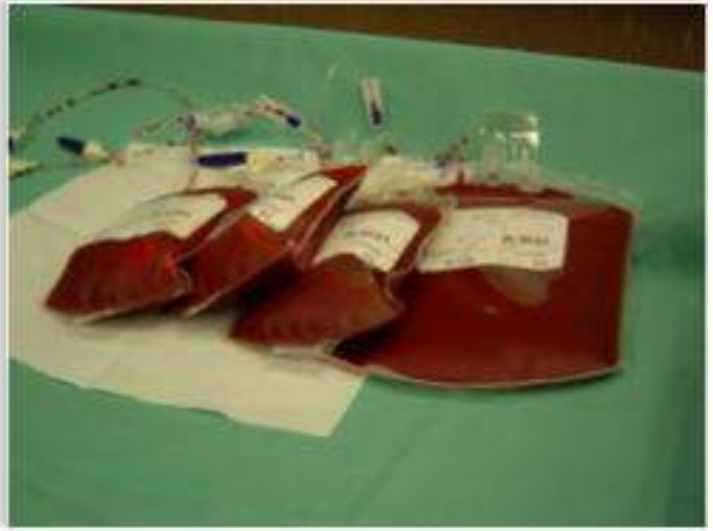






Passweg JR, Baldomero H, Bader P, et al. Hematopoietic stem cell transplantation in Europe 2014: more than 40 000 transplants annually. *Bone Marrow Transplant*. 2016;51(6):786–792.

Bone marrow

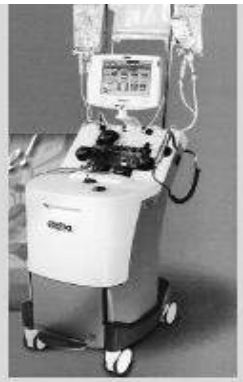


Cord blood

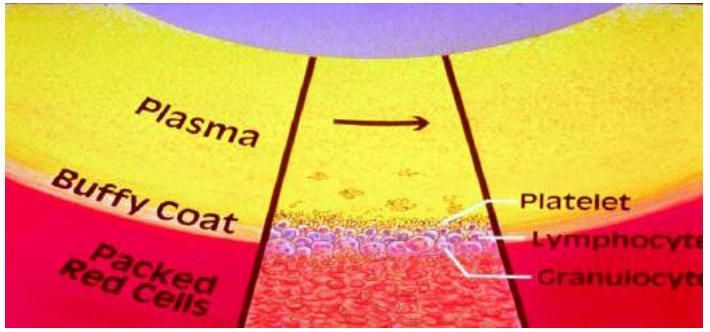
Cellule staminali da sangue periferico

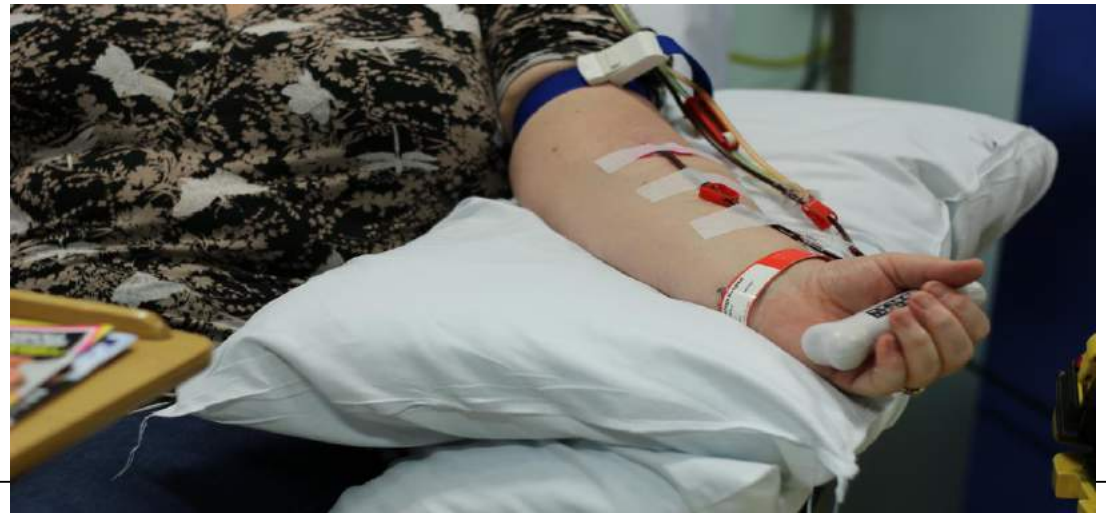
Cobe Spectra

Baxter Amicus



Spectra Optia





Mobilization and Apheresis Unit

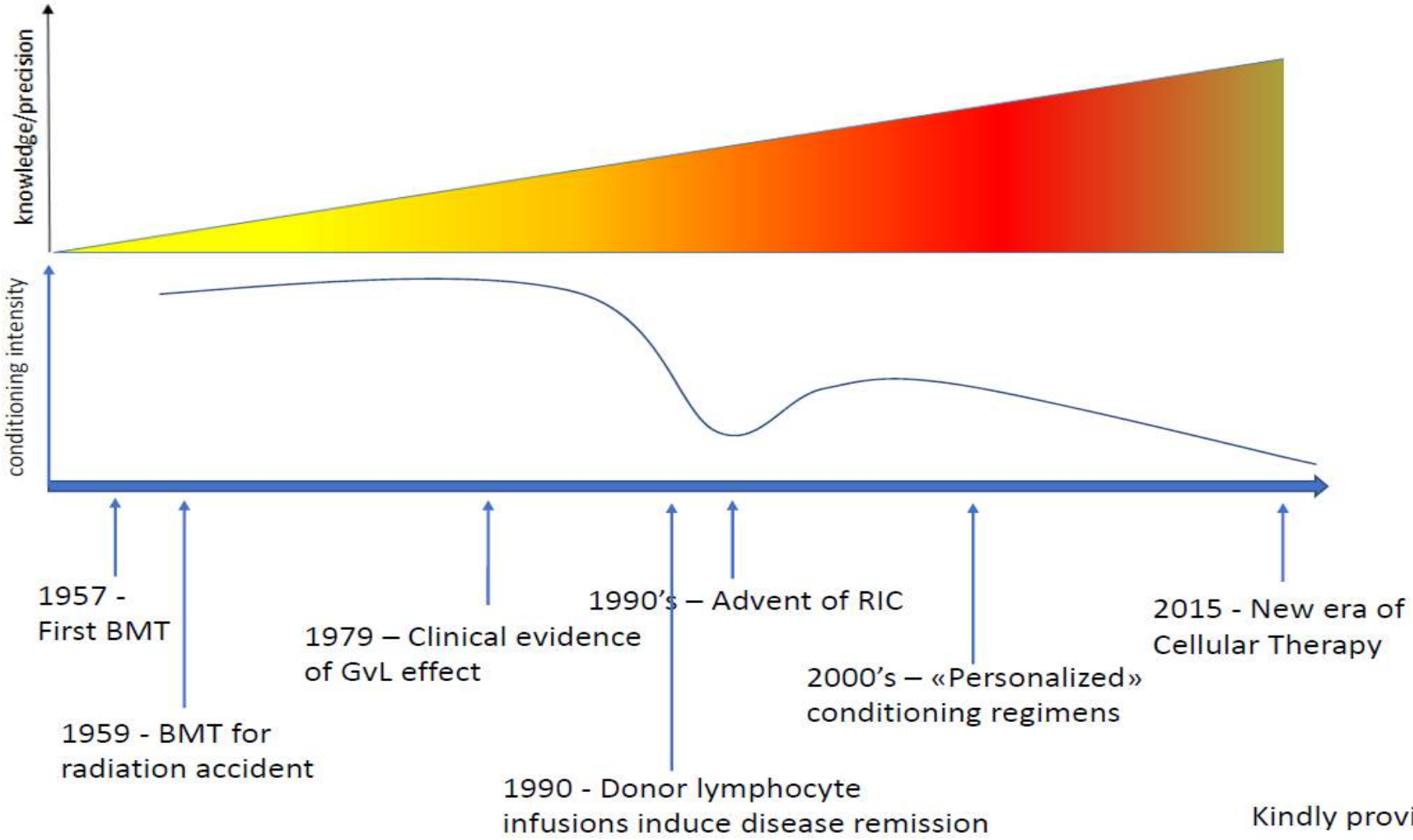
- assessment and clearance of the patient and donor in order to start the mobilization with granulocyte growth factor (G-CSF);
- Discuss the procedure and side effects with patient
- assessment of the patient and donor in order to start the procedure LAF or ECP or DLI (evaluation of CD34+ cells in PB)
- scheduling of leukapheresis and extracorporeal photochemotherapy;
- performing the leukapheresis, DLI/ ECP procedures.
- Lately schedule CAR-T collections and transports…
- Management of emergency situations

APHERESIS COLLECTION FACILITY STANDARDS

PART C

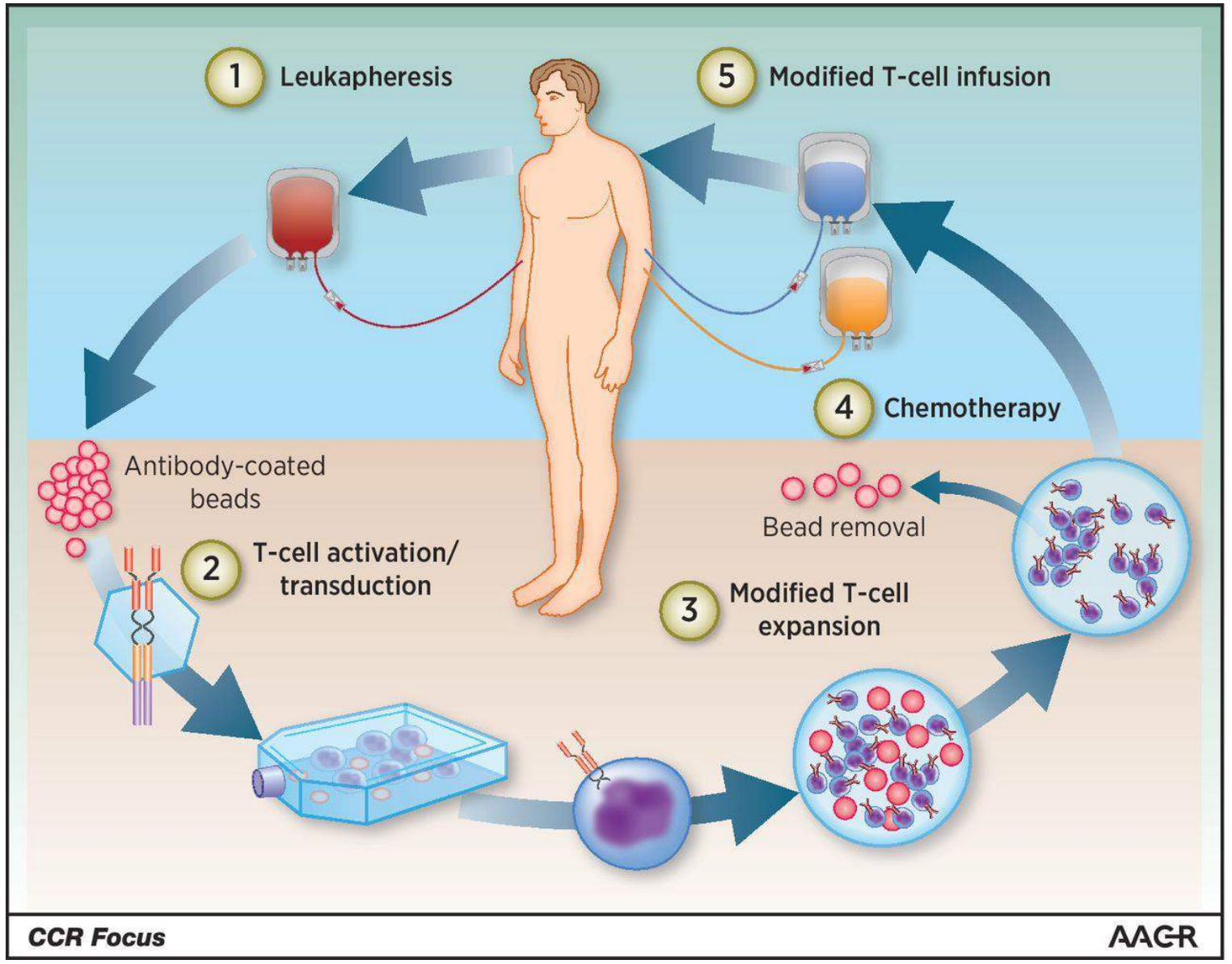
C1	General
C2	Apheresis Collection Facility
C3	Personnel
C4	Quality Management
C5	Policies and Standard Operating Procedures
C6	Allogeneic and Autologous Donor Evaluation and Management
C7	Coding and Labeling of Cellular Therapy Products
C8	Process Controls
C9	Cellular Therapy Product Storage
C10	Cellular Therapy Product Transportation and Shipping
C11	Records
C12	Direct Distribution to Clinical Program

Rapid BMT evolution history and impact on apheresis team



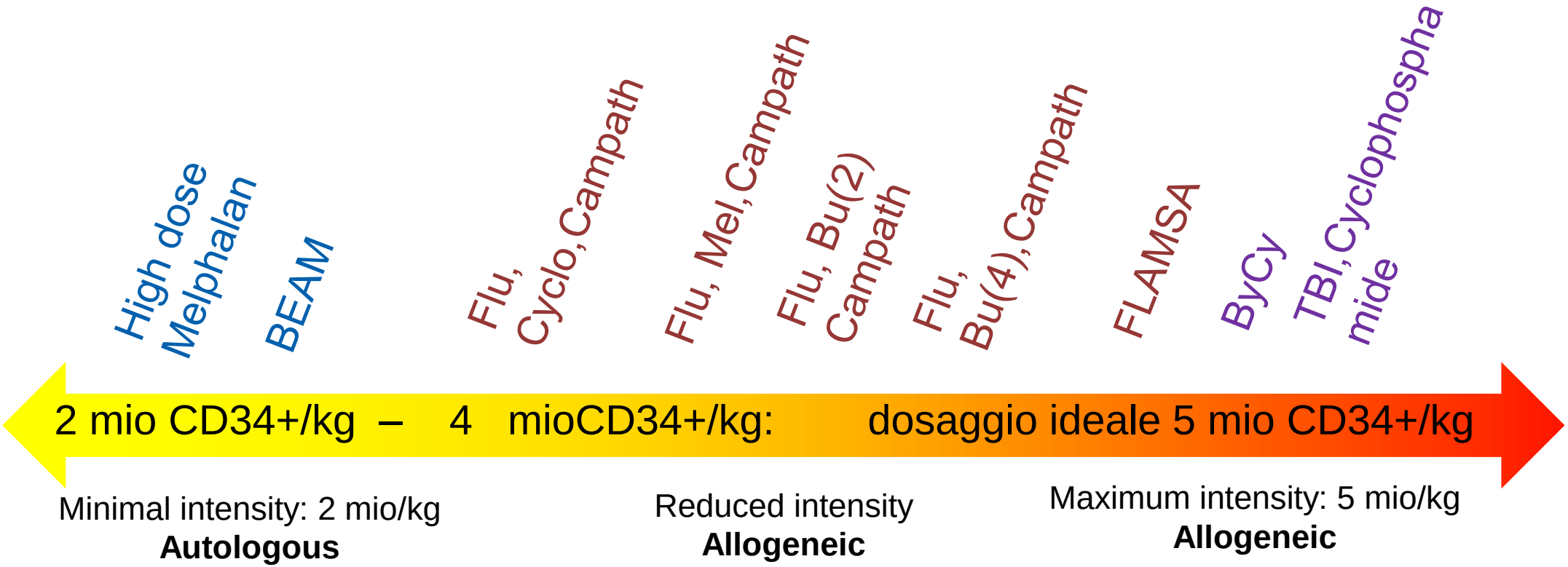
Kindly provided by R. Crocchiolo

CAR-T cell therapy



BMT related = PBSC collection target vary

PBSC Transplant Dose
autoPBSC ~ 2 (minimum) – 5(optimal) x 106 CD34+ cells/Kg
alloPBSC ~ 4 - 6 x 10^6 CD34+ cells/Kg
Haploidentical ~ protocol depending~ (4 x 106CD34+ cells/Kg)



CD34+ = A designation for human lymphocyte surface protein (antigen) recognized by CD34 antibodies. It identifies a population of mononuclear cells (MNCs) of which stem cells are a subset. Testing for this antigen marker is a way of measuring the quality of a stem cell collection.

Leukaferesi per CAR-T

- Lymphocyte collection if at least 0,4 Lymph.
- **Kite** requires **$2x10^9$ lymph**. Others (Novartis, Celgene) just **$1x10^9$.**
- Cell separator: Spectra Optia
- CMNC (continuous mononuclear cell collection) program.
- Same program as for stem cells but setting a lighter interphase (exactly as for photoferesis).
- Limit flow rate to 90cc/min takes **3 hours** to process 15 liters.

No age limit!

Pts selection

✓ **Leukaferesis**

Lymphocite T processing

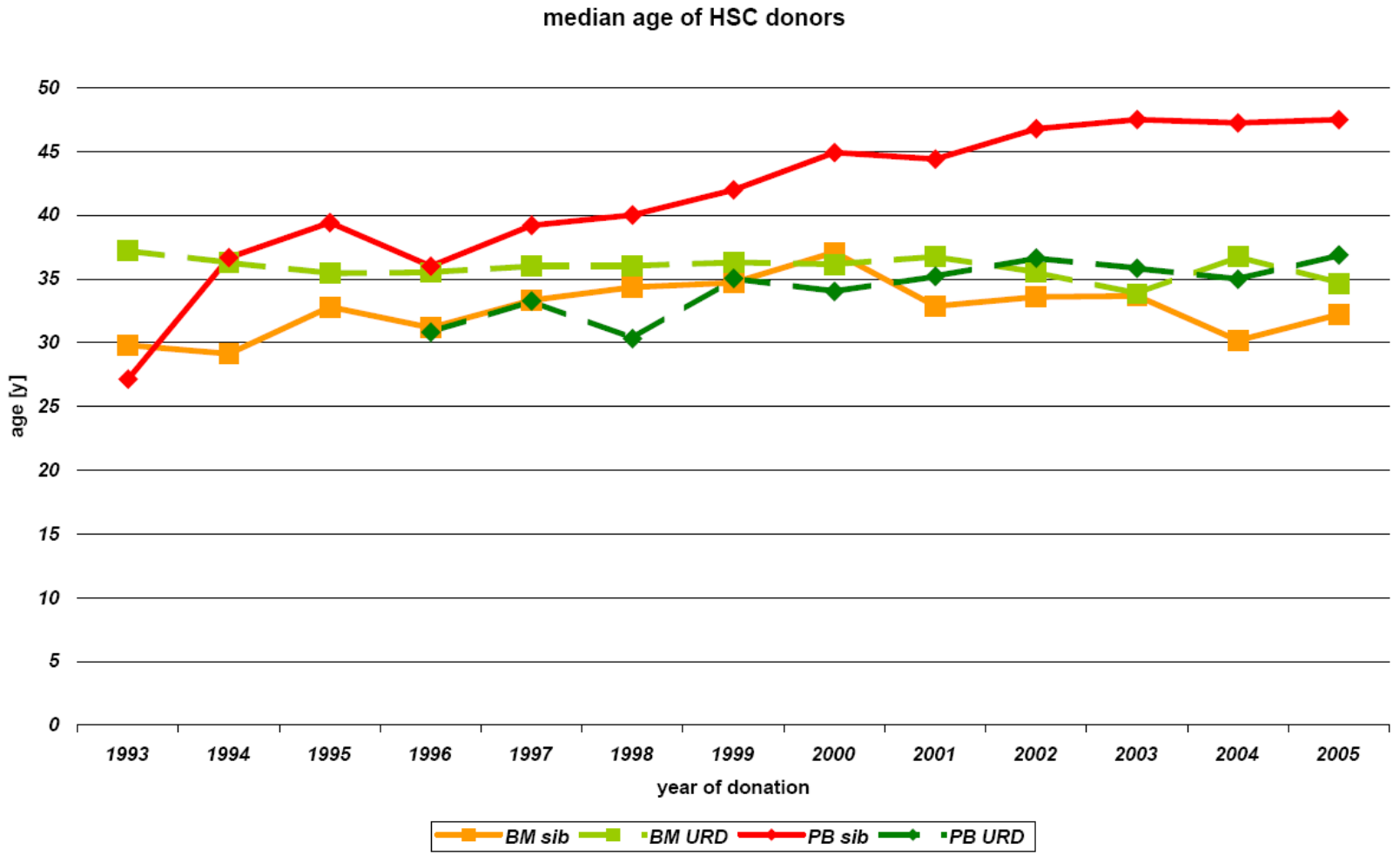
Recovey

Lymphodepletion

Reinfusion

Short term FU

Long term FU



Halter J et al. Hematologica 2009

Donation is not without morbidity and risk

- 5 donor fatalities
- 37 severe adverse events
- 20 hematologic malignancies

haematologica

the Hematology Journal
Open Access Publication

Severe events in donors after allogeneic hematopoietic stem cell donation

Joerg Halter[1], Yoshihisa Kodera[2], Alvaro Urbano Ispizua[3], Hildegard T. Greinix[4], Norbert Schmitz[5], Geneviève Favre[1], Helen Baldomero[6], Dietger Niederwieser[7], Jane F. Apperley[8] and Alois Gratwohl[1] for the European Group for Blood and Marrow Transplantation (EBMT) activity survey office

Published online before print December 4, 2008, doi: 10.3324/haematol.13668
haematol January 1, 2009 vol. 94 no. 1 94-101

» Abstract
Full Text
Full Text (PDF)

About the Jo
Editorial Boa
Policies and
Information
Information Reviewers

Serious adverse events after PBSC donation

Associated with biologic actions of G-CSF:

- Splenic ruptures
- Allergic reactions/anaphylaxis
- Immunomodulation/ Proinflammatory
  - Triggering of inflammatory diseases
- Thrombosis (arterial, venous)
- Respiratory distress/acute lung injury
- Sickle cell crisis

Halter J et al. 2009 Hematologica 2009 ,Miller JP et al. BBMT 2008, Favre G et al. BMT 2003,
De la Rubia J et al. Haematology 2008, Horowitz M, Confer D: Hematology 2005, Pulsipher MA et al. Blood 2009, Pulsipher M, et al, Blood 2013

Catheter-related:

- Bleeding, thrombosis, pneumo-/hematothorax

Related to apheresis procedure:

- Citrate toxicity/ Hypocalcemia
- Thrombocytopenia/anticoagulation
- Priming with allogeneic blood (paed)

Miller JP et al. BBMT 2008, Favre G et al. BMT 2003, De la Rubia J et al. Haematology 2008, Horowitz M, Confer D: Hematology 2005, Pulsipher MA et al. Blood 2009, Pulsipher M, et al, Blood 2013, Hirsch B et al., Blood 2011

Medical health history and donor evaluation

- Personal history, including allergies and prior experience with anesthesia
- exercise tolerance
- Neurologic, cardiovascular, respiratory or musculosceletal problems
- Back pain or lower extremity pain
- physical examination, including blood pressure and pulse
- ECG
- Pregnancy test
- Complete Blood Count
- Serum creatinine concentration
- Chest x-ray for patients over 50 years or those with suspected cardiac or pulmonary disease
- CT scan?
- Myocard perfusion imaging?

• Nurse challenges & Donation Procedure

Main side effects observed in the two types of donation

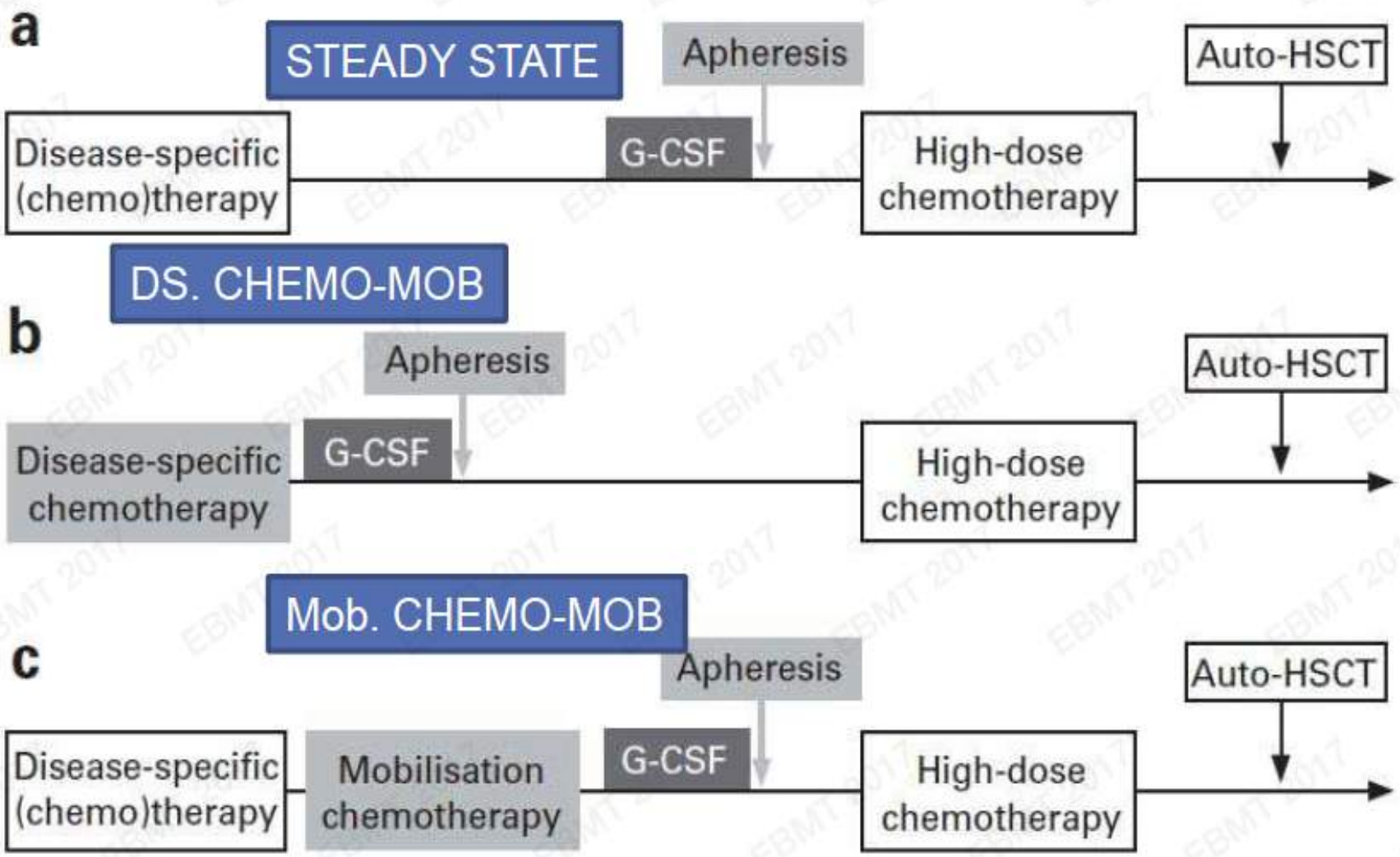
Bone marrow donation		PBSC donation	
Symptom	Percentage of donors who reported the side effect*	Symptom	Percentage of donors who reported the side effect**
Tiredness	80%	Bone pain	96%
Pain in the area of the collection	75%	Headache	78%
Pain in walking	71%	Myalgia	78%
Back ache	65%	Feeling of general discomfort	78%
Sore throat	60%	Insomnia	41%
Pain in sitting	59%	Nausea	33%
Pain in climbing stairs	50%	Flu-like symptoms	33%
Nausea	50%	Increased sweating	25%
Mild headache	45%	Anorexia	21%
Headache	35%	Chills	19%
Pain in the lumbar	29%	Fever	16%
Vomit	27%	Local reactions at the injection site	12%
Pain in the area of bandage	23%	Skin reactions	9%
Fever	22%	Vomit	8%
Haemorrhage at the collection sites	9%	Allergy	3%
Weakness	4%		

* **Source:** Data collected from the registry of bone marrow donors USA -NMDP from 11,084 subjects unrelated who donated bone marrow HSCs from 1989 to 2002;

cedure, type of
ascular access etc.

ıal distress, fatigue,
ache, hypotention,

g



Bone Marrow Transplantation (2014) 865 – 872

Kinds of Mobilisation strategies

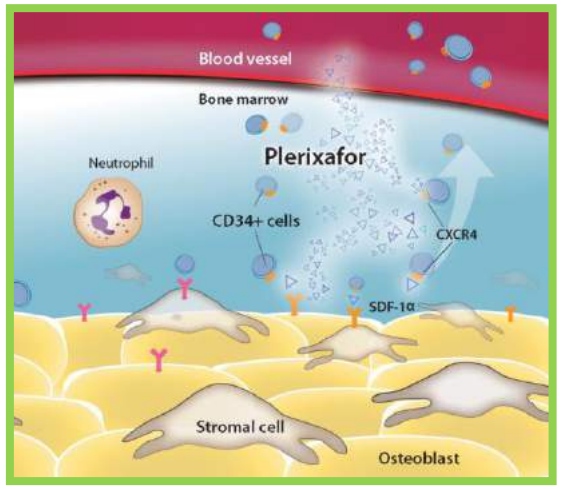
1. Growth factors alone
2. Chemotherapy + Growth factors (or cytokines)
3. Newer strategies (i.e. Biosimilars, Plerixafor....)

Risk Factors and Characteristics Associated with Poor Autologous Stem Cell Mobilization

- Type and amount of chemotherapy administered to patient prior to mobilization
- Advanced age (> 60 years)
- Multiple cycles of previous chemotherapy for treatment of underlying disease
- Radiation therapy
- Short time interval between chemotherapy and mobilization
- Extensive disease burden
- Refractory disease
- Tumour infiltration of bone marrow
- Prior use of lenalidomide
- Evidence of poor marrow function (e.g. low platelet and CD34+ blood count) at time of mobilization

• Mobilization with Plerixafor and/or GCSF only

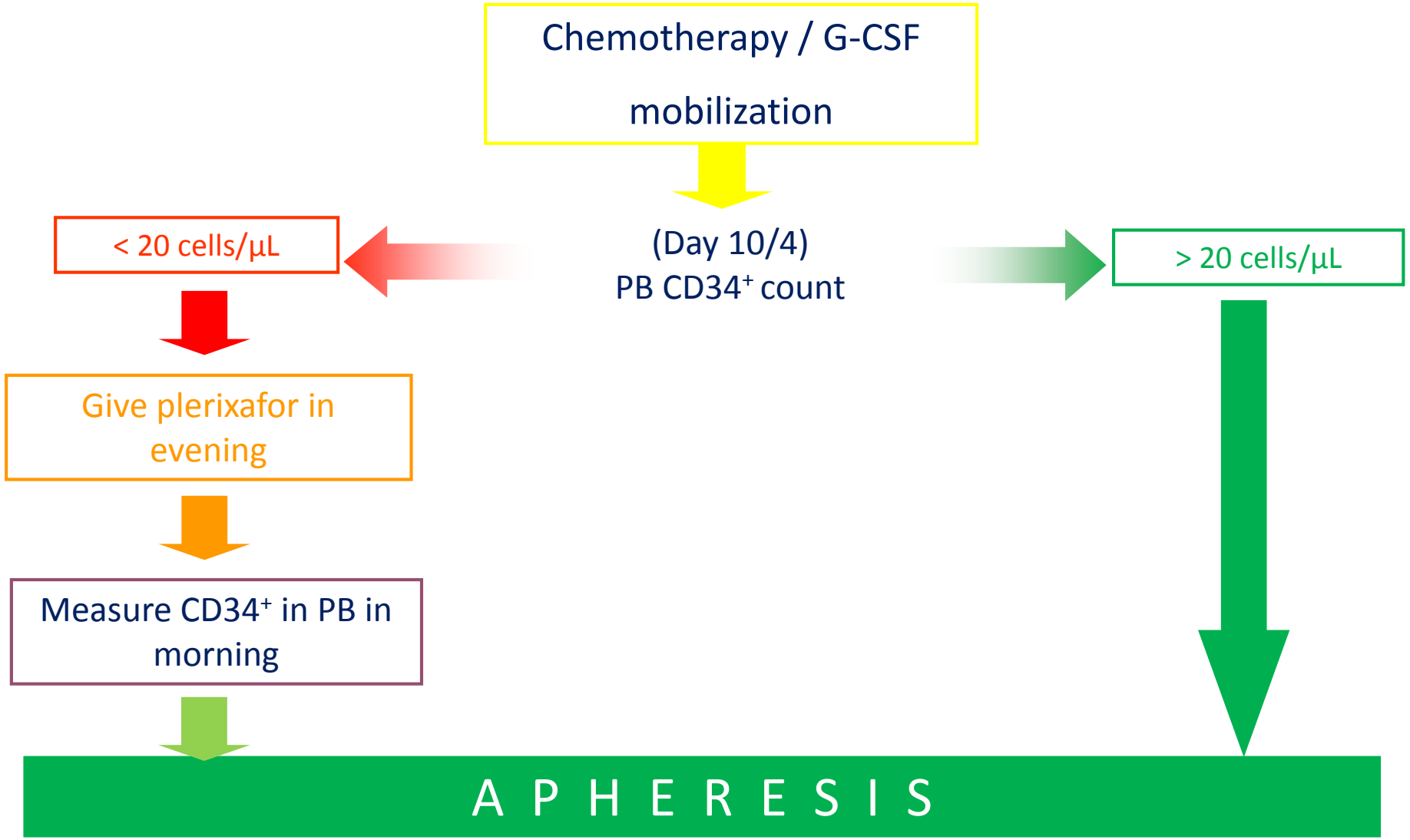
- Plerixafor is a novel agent that has been approved in the European Union for use in conjunction with G-CSF in lymphoma and multiple myeloma patients whose cells mobilise poorly, to mobilise stem cells from the bone marrow into the peripheral blood for collection and autologous transplantation
- Plerixafor is a small-molecule CXCR4 antagonist that reversibly inhibits the interaction between CXCR4 and SDF-1a
- Use of plerixafor in combination with G-CSF has been shown to improve CD34+ cell collections in lymphoma and multiple myeloma patients compared to G-CSF alone



Agent	Adverse events
Filgrastim	• Musculoskeletal pain
Lenograstim	• Bone & back pain • Leucocytosis & thrombocytopenia • Transient increases in liver function tests • Elevated LDH • Headache & asthenia (weakness)
Plerixafor	• Diarrhoea & nausea • Injection & infusion site reactions

Very Common (> 10%) Adverse Reactions Associated With Agents Used in Stem Cell Mobilization

Pre-emptive use of novel mobilizing agents in auto-SCT



Biosimilar G-CSF in mobilization

European Journal of Haematology 88 (154–158)

ORIGINAL ARTICLE

Plerixafor and Filgrastim XM02 (Tevagastrim®) as a first line peripheral blood stem cell mobilisation strategy in patients with multiple myeloma and lymphoma candidated to autologous bone marrow transplantation

Giovanna Andreola[1], Aleksandra Babic[1], Cristina Rabascio[2], Mara Negri[1], Giovanni Martinelli[1] and Daniele Laszlo[1]

[1]Stem Cell Collection Unit, [2]Laboratory of Haematology-Oncology, Haematoncology Division, European Institute of Oncology, Milan, Italy

Abstract

Plerixafor, a CXCR4 antagonist, has shown to be effective in increasing the number of circulating stem cells, even in patients failing a previous mobilisation attempt. Recently a number of non-glycosylated recombinant human granulocyte-colony stimulating factor (G-CSF) has been clinically approved for the same indications as the originator G-CSF for comparable safety and efficacy and their reduced cost. In an attempt to provide a less toxic strategy, 14 patients affected by haematological malignancies (non-Hodgkin's lymphoma = 4, Hodgkin's disease = 2 and multiple myeloma = 8), received the combination of biosimilar filgrastim and plerixafor as a first line mobilising strategy. The median number of circulating CD34+ cells on day 4 was 16 (3–42); Plerixafor was administered to all, but one patient who had already 42 CD34+ cells per μL on day 4. On day 5, after plerixafor administration, the median number of circulating CD34+ cells had raised to 60 per μL (14–138). All the patients underwent leukapheresis and were able to collect a number of CD34+ cells $\geq 2.0 \times 10^6$/kg in a median number of procedures of one. Although preliminary, these data show the combination of biosimilar filgrastim and plerixafor is effective and provides a non-toxic approach to mobilise stem cells.

• Mobilisation and apheresis unit – • nurse challenges

- How and when to administer agents used in the mobilisation process
- Schedule of chemotherapy used in the mobilisation process
- What medications the patient should and should not take during mobilisation
- Expected adverse events and their management for all agents used in mobilisation (together with inpatient unit)
- Review of care of catheter used for apheresis
- Explanation of apheresis procedure and expected adverse events
- Importance of laboratory monitoring and how to manage electrolyte imbalances
- Stem cell collection and target level
- Options for patients who mobilise poorly or fail to mobilise

Comparison of Mobilization Methods

Mobilisation regimen	Characteristics
Filgrastim or lenograstim	• Low toxicity • Outpatient administration • Can be self-administered • Reasonable efficacy in most patients • Predictable mobilisation, permitting easy apheresis scheduling • Shorter time from administration to collection compared to growth factor + chemotherapy • Bone pain • Lower stem cell yield compared to growth factor + chemotherapy
Filgrastim or lenograstim + chemotherapy	• Higher stem cell yield compared to growth factor alone • Fewer stem cell collections • Potential for anticancer activity • May impair future mobilisation of stem cells • May require hospitalisation • Associated with increased numbers of side effects • Inconsistent results • Longer time from administration to collection compared to growth factor • Low predictability of time to peak peripheral blood CD34+ cell levels
Filgrastim or lenograstim + plerixafor	• Low toxicity • Outpatient administration • Low failure rate • High probability of collecting optimal number of CD34+ cells • Efficacy in poor mobilisers • Predictable mobilisation permitting easy apheresis scheduling • Shorter time from administration to collection compared to growth factor + chemotherapy • Gastrointestinal adverse affects

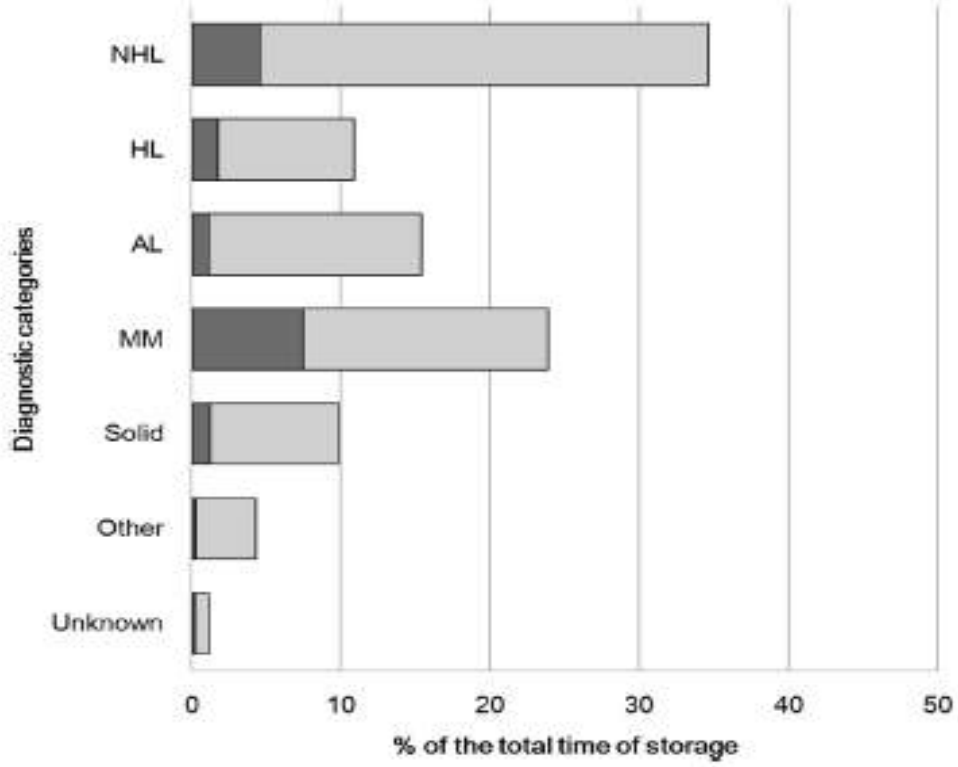
PBSC Collection Goals

- Collect a product with
- High – adequate - PBSC counts
  - Low cross-cellular contamination (RBC, Plt, ANC)
  - Small collect volume
- In as few procedures as possible to
  - ↓ costs
  - ↑ patient comfort
- Ensure patient safety

TODAY's Problem - OCCUPACY OF DEPOSITORY

- 83.4% of the depositories occupancy correspond to useless storage, the reamaining 16.6% to useful storage.

Figure 4. Relative proportion of "useful" (dark gray) and "useless" (light gray) storage across diagnostic categories. Data are expressed in percentage of the total amount of SCU-years analyzed in the study.



! **Storing costs:**

65-100$/year/unit

Kinetics of the use of cryopreserved autologous stem cell grafts: a GITMO-SIDEM survey

useful
useless

International Society for Cellular Therapy ISCT

Cytotherapy, 2014; 16: 101–110

JACOPO OLIVIERI[1], LUCA PIERELLI[2], MARTINO INTRONA[3], PATRIZIA ACCORSI[4], ALBERTO BOSI[5], PAOLO PERSEGHIN[6], MARCO RISSO[7], ANNINO PANDOLFI[2], STEFANIA MANCINI[1], MONIA MARCHETTI[8], SIMONE DAL POZZO[5], ELISA GOTTI[3], ALESSANDRO RAMBALDI[3], PIETRO LEONI[1] & ATTILIO OLIVIERI[1], ON BEHALF OF THE GITMO (GRUPPO ITALIANO TRAPIANTO DI MIDOLLO OSSEO)–SIDEM (SOCIETÀ ITALIANA DI EMAFERESI E MANIPOLAZIONE CELLULARE) WORKING GROUP ON SCU DISPOSAL

PBSC Collection Timing

Good timing avoids:

- Unnecessary collection procedures
- Unnecessary PBSC processing
- Saves freezing space
- Reduces cost (procedure, processing, growth factors)
- Saves the patient time and discomfort, reduces side effects during the transfusion

PBSC Collection Timing

Determination of the best timing :

- Growth factor mobilization (some MM pts and donors):

  First collection procedure ~ day 4 - 5 (peak of CD34+ cell count)

- Cytotoxic drugs and growth factors (some MM pts, NHL, HD) :

  Peak of CD34+ cell count varies after chemotherapy mobilization 12-15 day

  First collection determined by:

  – WBC count
  – CD34+ cell count

CLINICAL APHERESIS UNIT
The Beatson West of Scotland Cancer Centre

Telephone: 0141 301 7013/7014
Fax: 0141 301 7022

TABLE OF USUAL DAY OF FIRST PBSC COLLECTION DEPENDING ON MOBILISING CHEMOTHERAPY

Chemotherapy Regime	Recommended day to start chemo	Start GCSF (1st day of Chemo = day 0)	Average Rebound Day
CHOP	Friday	3	10
Cyclo 1.5g/m^2 or 2 g/m^2	Monday	1	9
Cyclo 3g/m^2 or 4 g/m^2	Friday	1	10
Cyclo 6 g/m^2 or 7 g/m^2	Wednesday	7	14
Cytarabine 6 g/m^2	Friday	4 or 7	17-19
DAT	No preference	16	20
DHAP	Wednesday	8	13
ESHAP	Wednesday	7	13
IVAC	Wednesday	6	14
IVE	Wednesday	5	13
MACE	No preference	13	16-26
H.D. Methotrexate	Tuesday	4	8-10
MIDAC	No preference	10	24
TIP	Friday	6	11
VIDE	Tuesday	5	14

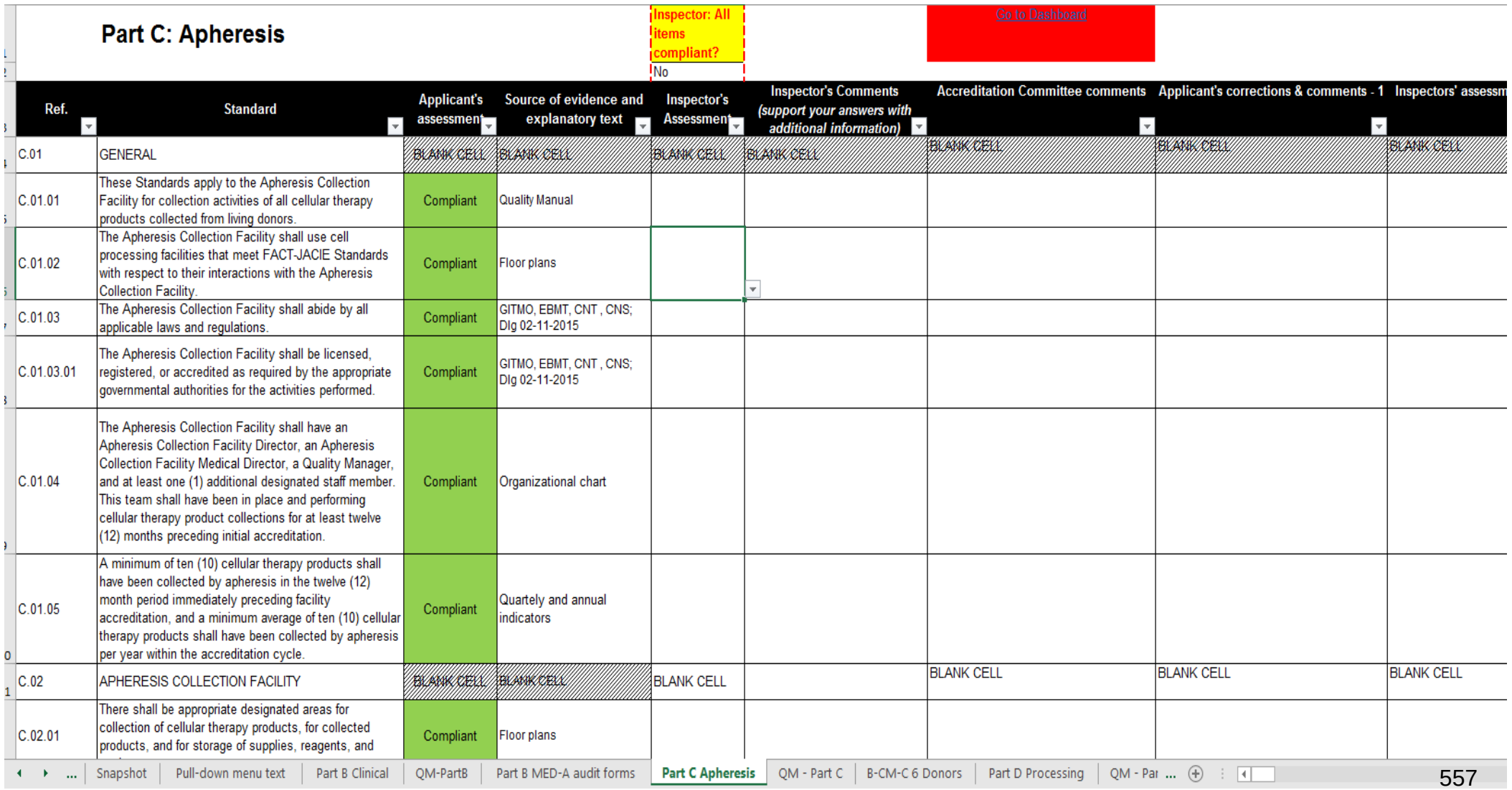
Please consider date of commencing chemotherapy carefully.
NB There is no weekend or public holiday processing service available

Courtesy of Kenny Douglas

standards

- **C2: APHERESIS COLLECTION FACILITY**
- C2.1 There shall be appropriate designated areas for collection of cellular therapy products, for
- collected products, and for storage of equipment, supplies, and reagents.
- C2.1.1 The Apheresis Collection Facility shall be divided into defined areas of adequate
- size to prevent improper labeling, mix-ups, contamination, or cross-contamination
- of cellular therapy products

- C2.1.2 There shall be a designated area for collection with appropriate location and
- adequate space and design to minimize the risk of airborne microbial
- contamination.
- C2.1.3 There shall be a process to control storage areas to prevent mix-ups,
- contamination, and cross-contamination of all cellular therapy products.
- C2.1.4 There shall be suitable space for confidential donor examination and evaluation.



Part C: Apheresis

Inspector: All items compliant? No

Go to Dashboard

Ref.	Standard	Applicant's assessment	Source of evidence and explanatory text	Inspector's Assessment	Inspector's Comments *(support your answers with additional information)*	Accreditation Committee comments	Applicant's corrections & comments - 1	Inspectors' assessm
C.01	GENERAL	BLANK CELL	BLANK CELL	BLANK CELL	BLANK CELL	BLANK CELL	BLANK CELL	BLANK CELL
C.01.01	These Standards apply to the Apheresis Collection Facility for collection activities of all cellular therapy products collected from living donors.	Compliant	Quality Manual					
C.01.02	The Apheresis Collection Facility shall use cell processing facilities that meet FACT-JACIE Standards with respect to their interactions with the Apheresis Collection Facility.	Compliant	Floor plans					
C.01.03	The Apheresis Collection Facility shall abide by all applicable laws and regulations.	Compliant	GITMO, EBMT, CNT , CNS; Dlg 02-11-2015					
C.01.03.01	The Apheresis Collection Facility shall be licensed, registered, or accredited as required by the appropriate governmental authorities for the activities performed.	Compliant	GITMO, EBMT, CNT , CNS; Dlg 02-11-2015					
C.01.04	The Apheresis Collection Facility shall have an Apheresis Collection Facility Director, an Apheresis Collection Facility Medical Director, a Quality Manager, and at least one (1) additional designated staff member. This team shall have been in place and performing cellular therapy product collections for at least twelve (12) months preceding initial accreditation.	Compliant	Organizational chart					
C.01.05	A minimum of ten (10) cellular therapy products shall have been collected by apheresis in the twelve (12) month period immediately preceding facility accreditation, and a minimum average of ten (10) cellular therapy products shall have been collected by apheresis per year within the accreditation cycle.	Compliant	Quartely and annual indicators					
C.02	APHERESIS COLLECTION FACILITY	BLANK CELL	BLANK CELL	BLANK CELL		BLANK CELL	BLANK CELL	BLANK CELL
C.02.01	There shall be appropriate designated areas for collection of cellular therapy products, for collected products, and for storage of supplies, reagents, and	Compliant	Floor plans					

Snapshot | Pull-down menu text | Part B Clinical | QM-PartB | Part B MED-A audit forms | Part C Apheresis | QM - Part C | B-CM-C 6 Donors | Part D Processing | QM - Par ...

Part C: Apheresis

Inspector: All items compliant? No

Go to Dashboard

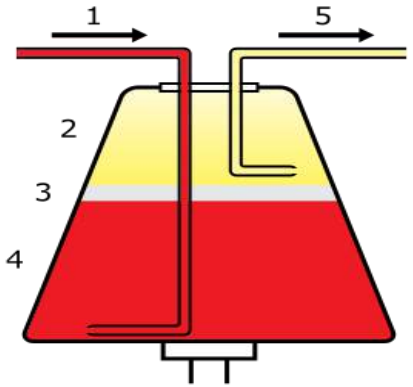
Ref.	Standard	Applicant's assessment	Source of evidence and explanatory text	Inspector's Assessment	Inspector's Comments *(support your answers with additional information)*	Accreditation Committee comments	Applicant's corrections & comments - 1	Inspectors' assessr
C.04.14.03	Changes to a process shall include evaluation of risk to confirm that they do not create an adverse impact anywhere in the operation and shall be validated or verified as appropriate.	Compliant	POS T.851.01 Procedura Convalida e change control					
C.06	ALLOGENEIC AND AUTOLOGOUS DONOR EVALUATION AND MANAGEMENT	See separate worksheet 'B-CM-C Donors'	BLANK CELL	BLANK CELL		BLANK CELL	BLANK CELL	BLANK CELL
C.07	CODING AND LABELING OF CELLULAR THERAPY PRODUCTS	BLANK CELL	BLANK CELL	BLANK CELL		BLANK CELL	BLANK CELL	BLANK CELL
C.07.01	ISBT 128 CODING AND LABELING	BLANK CELL	BLANK CELL	BLANK CELL		BLANK CELL	BLANK CELL	BLANK CELL
C.07.01.01	Cellular therapy products shall be identified according to the proper name of the product, including appropriate attributes, as defined in ISBT 128 Standard Terminology for Blood, Cellular Therapy, and Tissue Product Descriptions.	Compliant	SEC, UNI, POS T.852.01 ETICHETTATURA PRODOTTI CELLULARI, ELIOT SOFTWARE					
C.07.01.02	If coding and labeling technologies have not yet been implemented, the Apheresis Collection Facility shall be actively implementing ISBT 128.	Partially compliant	Implementing SEC					
C.07.02	LABELING OPERATIONS	BLANK CELL	BLANK CELL	BLANK CELL		BLANK CELL	BLANK CELL	BLANK CELL
C.07.02.01	Labeling operations shall be conducted in a manner adequate to prevent mislabeling or misidentification of cellular therapy products, product samples, and associated records.	Compliant	SEC, UNI, POS T.852.01 ETICHETTATURA PRODOTTI CELLULARI, ELIOT SOFTWARE					
C.07.02.01.01	Stocks of unused labels representing different products shall be stored in a controlled manner to prevent errors.	Not applicable						
C.07.02.01.02	Obsolete labels shall be restricted from use.	Not applicable						
C.07.02.02	Pre-printed labels shall be held upon receipt from the manufacturer pending review and proofing against a copy or template approved by the Apheresis Collection Facility Director or designee to confirm accuracy	Compliant	Institutional Procedures					

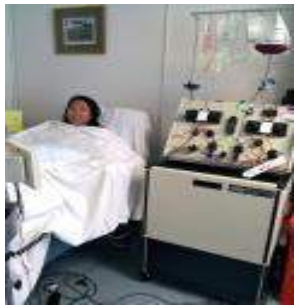
Apheresis : nurse challenges

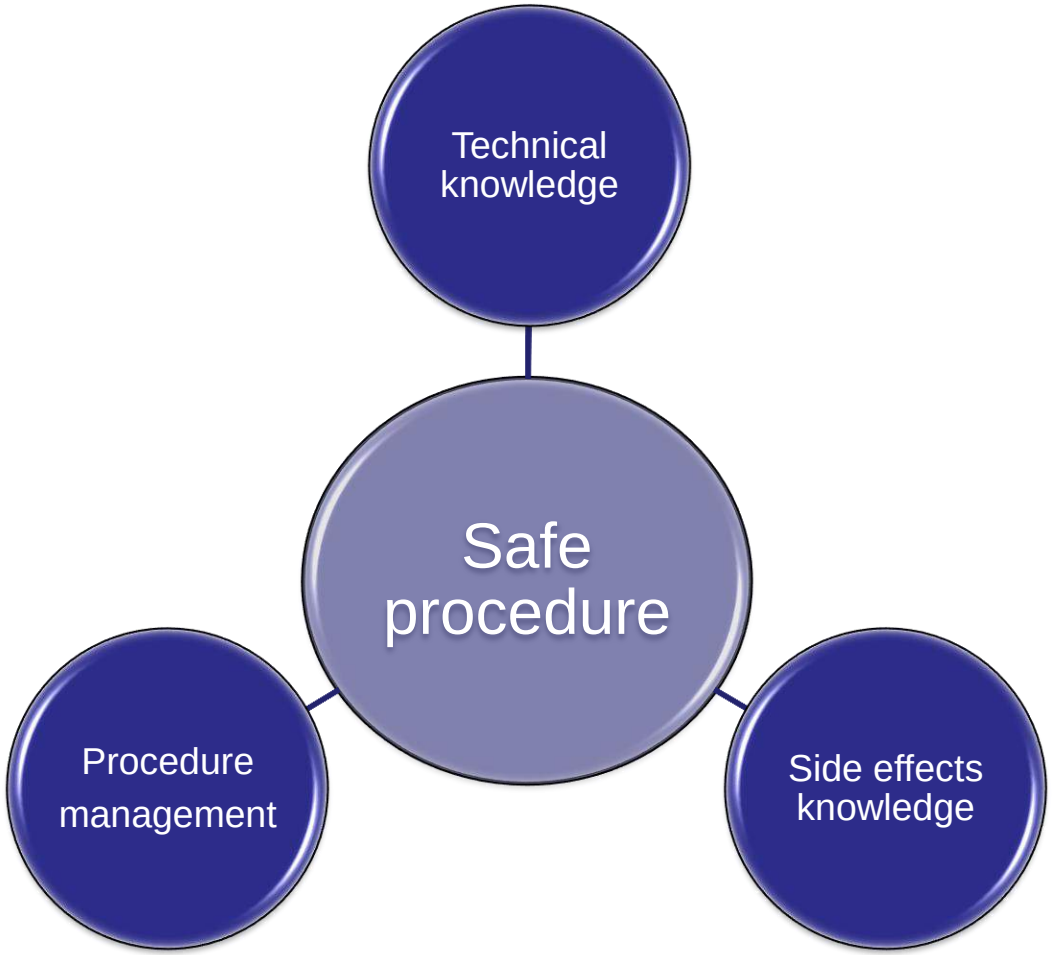
- Vascular access management - evergreen
- Nurses competences and competencies maintanance:
- Patient information
- Written consent

Apheresis machine

Complex but safe procedure….







Common Apheresis Complications

Adverse event	Cause	Signs & symptoms	Corrective action
Citrate toxicity	Anticoagulant (citrate) given during apheresis	*Hypocalcaemia* **Common:** dizziness & tingling in mouth area, hands & feet **Uncommon:** chills, tremors, muscle twitching & cramps, abdominal cramps, tetany, seizure, cardiac arrhythmia	Slow the rate of apheresis; increase the blood:citrate ratio; calcium replacement therapy
		Hypomagnesaemia **Common:** muscle spasm or weakness **Uncommon:** hypotonia & cardiac arrhythmia	Slow the rate of apheresis; increase the blood:citrate ratio; magnesium replacement therapy
		Hypokalaemia **Common:** weakness **Uncommon:** decrease in respiration rate	Slow the rate of apheresis; increase the blood:citrate ratio; potassium replacement therapy
		Metabolic alkalosis **Common:** worsening of hypocalcaemia **Uncommon:** decrease in respiration rate	Slow the rate of apheresis; increase the blood:citrate ratio
Thrombocytopenia	Platelets adhere to internal surface of the apheresis machine	Low platelet count, bruising, bleeding	Slow the rate of apheresis; increase the blood:citrate ratio
Hypovolaemia	Patient intolerant of large shift in extracorporeal blood and plasma volumes	Dizziness, fatigue, light-headedness, tachycardia, hypotension, diaphoresis, cardiac arrhythmia	Slow rate of apheresis session or temporarily stop it; intravenous fluid boluses
Catheter malfunction	Blood clot forms of catheter is not well positioned to allow for adequate blood flow	Inability to flush catheter, fluid collection under skin around catheter site, pain & erythema at catheter site; arm swelling, decrease in blood flow	Reposition the catheter; gently flush catheter; treat blood clot
Infection	Microbial pathogens enter bloodstream through catheter or catheter site	Fever, chills, fatigue, red & erythematous skin around catheter; hypotension, position blood cultures	Administer antibiotics; possibly remove catheter

Summary : Adverse Events

Minor
- Simptomatic hypocalcemia
- Circuit coagulation
- Puncture site haematoma
- Flow Failure - interruption

Average
- Allergic reaction-hypersensitivity
- Thrombosis of vein in use
- Nausea/Vomiting
- Fever with shiver

Serious
- Shock
- Vagal reaction
- Hemolysis
- Conduction or rhythm disorders
- Pulmonary edema

Local (linked to venous access)
- Injuries of vein
- Nervous injuries
- Tendon injuries
- Local allergic reaction
- Infections or thrombophlebitis

Systemic
- Related to a person
- Related to a separator
- Related to the procedure

Problems classification

➢Hardware

- Malfunctioning Instrument
- Disposable deviance

➢Procedural

- Related to patient
  - Citrate reaction– Hypotension –Vasovagal reaction – Allergic reaction
- Related to procedure management
  - Low CD34+ outcomes + Cross Cellular contamination

Total blood volume

- 5 liter

ECV

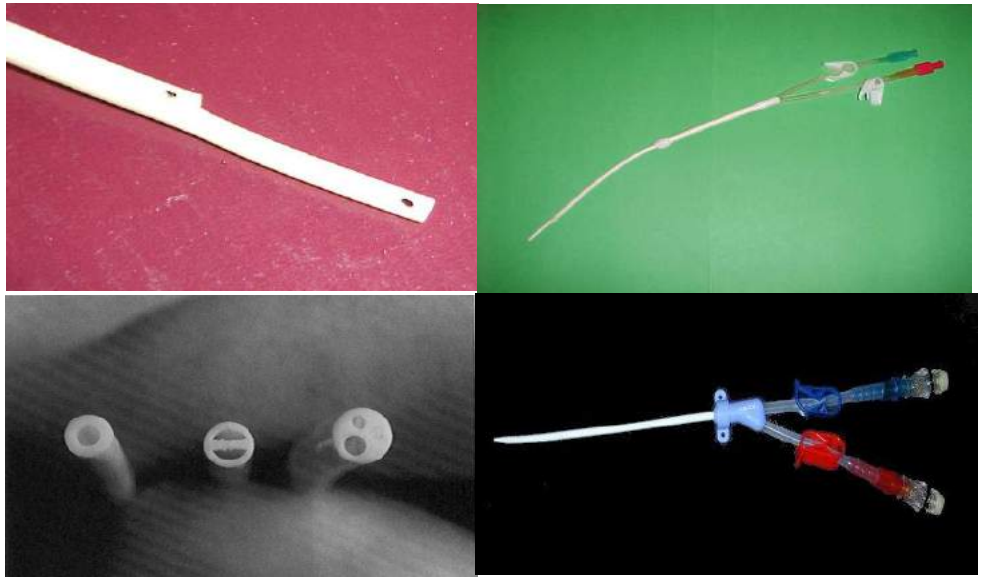
- Maximally 15% of TBV
- Important to know:
  - Volume disposable
  - Volume to collect
  - Tubes collected
  - TBV patient / donor

Age group	Approximate blood volume (mL/Kg)
Premature infant, at birth	90-105
Term newborn infant	80-90
Children > 3 months	70-75
Adolescents and adults Male Female	 70 65

Vascular access

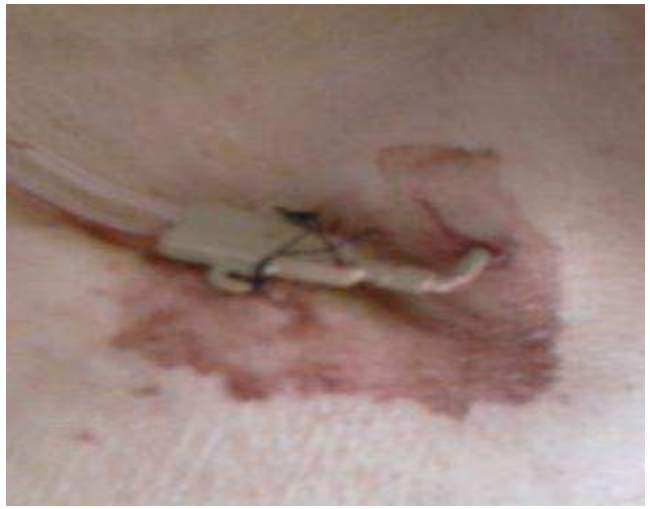
- Adequate vascular access mandatory for stabile blood flow

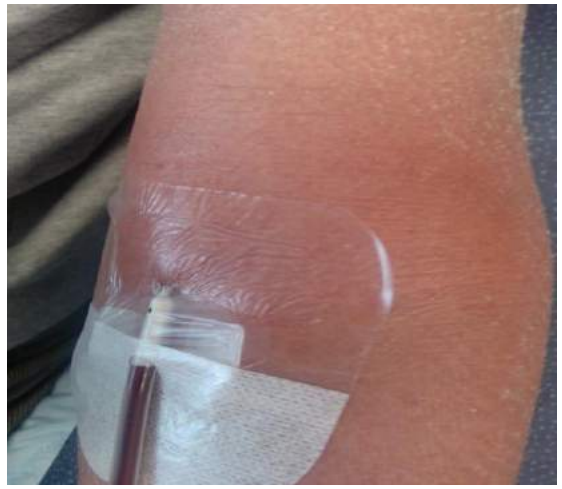
- Disease status
- Number of prior chemotherapy cycles
- Prior radiation therapy
- Age

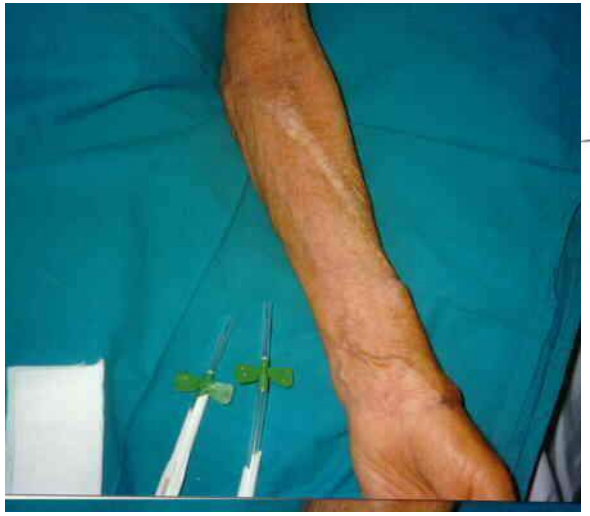


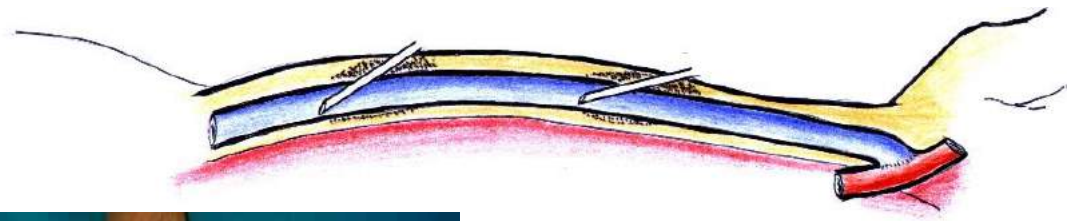
• Drawing problems

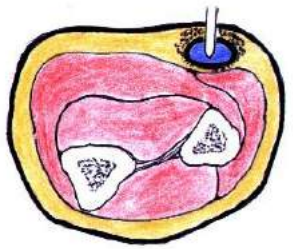
- If drawing pressure is low
- Catheter position needs to be verified









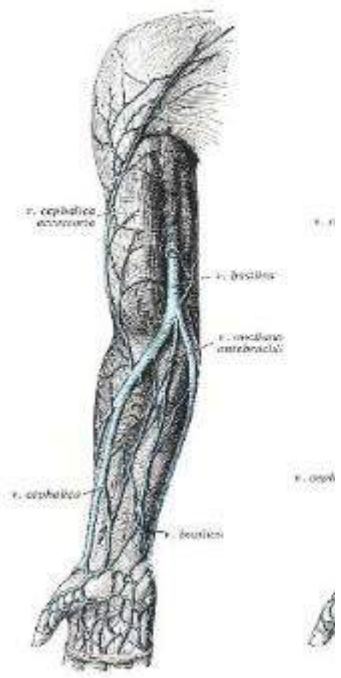


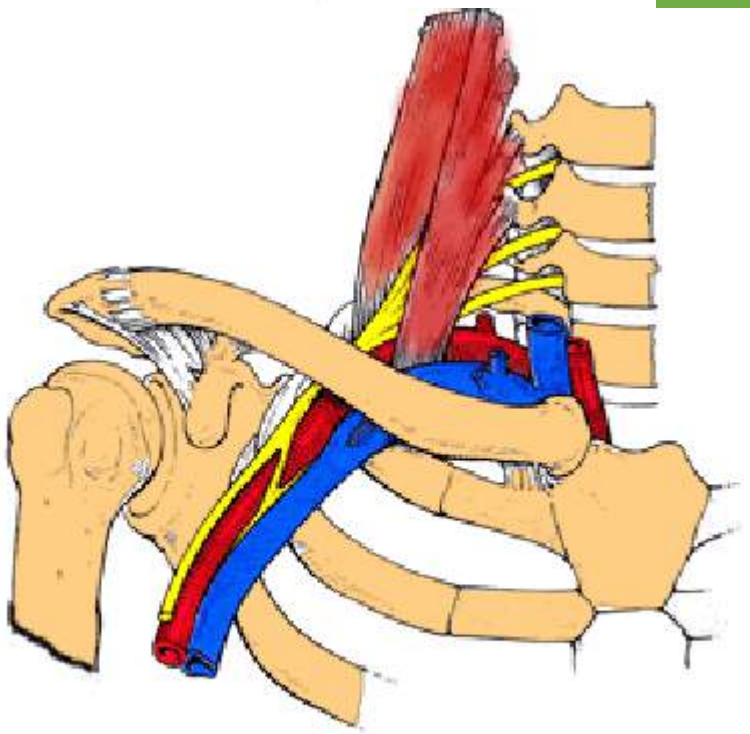
- Site of position vs catheter type

Frequent venous variations

Venipu

- Forearm
- Fossa C
- Subclav
- Internal
- Femora





Neyrinck & Vrielink - Febr 2015

Vascular Access

Donor:

- Anticubital access/return
- Forearm or hand return

ECP Procedures:

- Anticubital veins Access/Return
- 14 F lumen catheter
- Femoral, subclavian, jugular
- Fistula
- Graft

Patient:

- Anticubital Access/Return
- Forearm or hand return
- Femoral
- Subclavian
- Jugular
- Fistula
- Graft
- Port -a-Cath

TABLE III. A Comparison of the Advantages and Disadvantages Associated With Vascular Access Types Used in Therapeutic Apheresis (TA) Procedures

Vascular access type	Indications for use	Advantage	Complications
Peripheral Veins	Centrifugal based TA Acute or intermittent TA	Low rate of infections Immediate use	Patient discomfort Infiltration and sclerosis of veins
Non-tunneled central venous catheters	Short term use only (<2 weeks) Acute or intermittent TA Centrifugal or filter based TA	Easy to place at bedside Blood flow rate high	Risks inherent to catheter insertion Dysfunction Infection, including sepsis, and metastatic infections Central vein stenosis
Tunneled central venous catheters	Short or long term use	Reduced infection rate when compared to non-tunneled catheters	Risks inherent to catheter insertion
	Centrifugal or filter based TA	Blood flow rate high	Dysfunction Infection, including sepsis, and metastatic infections Central vein stenosis
Arteriovenous Fistula (AVF)	Chronic TA (>3 months) Centrifugal or filter based TA	Lowest infection and dysfunction rates compared to other vascular access types	Requires surgery and adequate patient vascular anatomy Requires a maturation period before use (~6–8 weeks) May be associated with primary maturation failure and subsequent need for additional procedures Requires trained staff for cannulation
Arteriovenous grafts (AVG)	Chronic TA (> 3 months) Centrifugal or filter based TA	Lower infection and dysfunction rates compared to catheters Most AVGs may be used within 2 weeks of placement	Requires surgery Requires trained staff for cannulation Higher infection/thrombosis rates compared to AVFs

J Clin Apher. 2013 Feb;28(1):64-72. doi: 10.1002/jca.21267.
Vascular access in therapeutic apheresis: update 2013.
Golestaneh L1, Mokrzycki MH.

Consideration for selecting vascular access in therapeutic apheresis (TA)

- The type of TA procedure prescribed and desired blood flow rate (ECP? PBSC? DLI?)
- The patient's vascular anatomy, mobility and hygiene.
- The acuity, frequency and anticipated duration of TA as determined by the underlying disease state and response to treatment.

J Clin Apher. 2013 Feb;28(1):64-72. doi: 10.1002/jca.21267.
Vascular access in therapeutic apheresis: update 2013.
Golestaneh L1, Mokrzycki MH.

The choice of vascular access for therapeutic apheresis
Kambiz Kalantari*
Article first published online: 26 APR 2012

Summarizing: PBSC collection procedure

- Major source for graft procurement in both autologous and allogeneic setting.
- The success of the procedure depends also on the use of adequate vascular accesses.
- Well- sized peripheral veins are the first option in autologous and allogeneic donations.
- Proper vascular access consent a blood flow-rate of about 40/100 ml per minute for both inlet and return lines.
- During PBSC collection, blood flow-rate is a key factor which improves collection efficiency and speed

C3.4.2 For Apheresis Collection Facilities collecting cellular therapy products from pediatric donors, physicians and collection staff shall have documented training and experience in performing these procedures.

C4.4 The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures addressing personnel requirements for each key position in the Apheresis Collection Facility. Personnel requirements shall include at a minimum:

C4.4.1 A current job description for all staff.

C4.4.2 A system to document the following for all staff:

C4.4.2.1 Initial qualifications.

C4.4.2.2 New employee orientation.

C4.4.2.3 Initial training and retraining when appropriate for all procedures performed.

C4.4.2.4 Competency for each critical function performed.

C4.4.2.5 Continued competency at least annually.

C4.4.2.6 Continuing education.

Apheresis nurse competences

1. Demonstrate the ability to assist the donor before, during and after the apheresis procedure
2. Recognize and effectively deal with adverse events
3. Manage fluid volumes during the apheresis procedure
4. Evaluate peripheral access and manage central and peripheral venous accesses
5. Demonstrate the ability to install the kit, perform priming and remove the appropriate kit for the apheresis procedure
6. Ability to perform the aphaeretic procedure independently
7. Being autonomous in the management of alarm systems of the cell separator in use
8. Demonstrate the ability to coordinate the entire aphaeretic procedure
9. Guarantee autonomy in starting, executing and terminating the aphaeretic procedure and in the management of care and assistance to the donor

Definitions

- Basic Training: route that leads to the skills acquisition in order to obtain new or better "performance”
- Educational Training: the set of all activities, including basic training aimed to develop and enrich the staff on the technical, specialist, managerial and cultural side.
- Competence: the proven ability to use knowledge and skills.
- Competency maintenance: the minimum activity set that needs to be performed by each operator in order to keep the assessments defined in the specific job-description.
- Competency Matrix: The activities carried out must be recorded in order to perform an annual assessment quantitative and qualitative for the activities that can be recognized.

Rationale for the definition of personnel training and training activities

- Define the methods of planning, implementation, management and registration of the activities of training, retraining, maintenance of skills and assessment of staff working within the structures involved in the activity of apheresis, with particular regard to the transplantation of CSE.
- Manage training schedule and delivery activities so that:

  - each operator is adequately trained and maintenance is guaranteed
  - the maintenance over time and skills evaluation regularly
  - integrating hospital SOPs

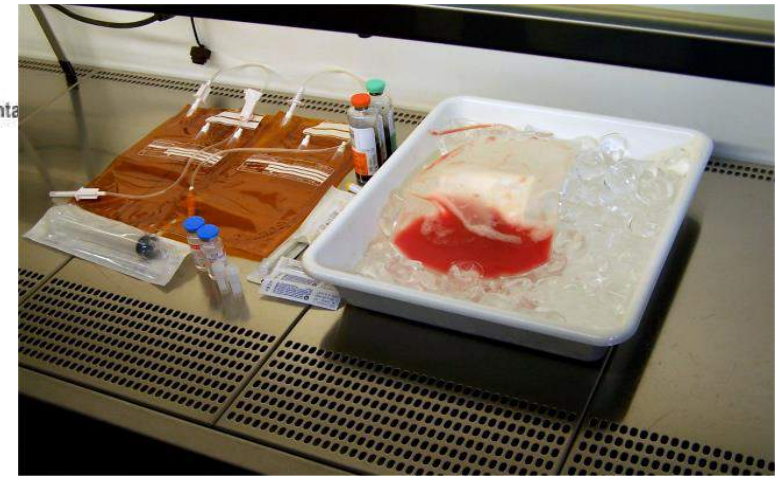
Cryopreservation

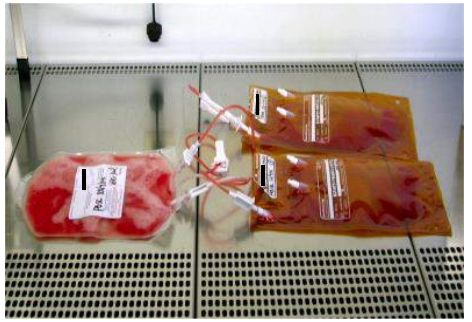
- PBSC AND BM can be stored for decades
- Liquid nitrogen excellent for long-term storage (controlled freezing) in tanks
- -70-80 ° C back-up freezer OK for storage up to 6 months
- 10% (lately 5-7%) DMSO used as a cryopreserve

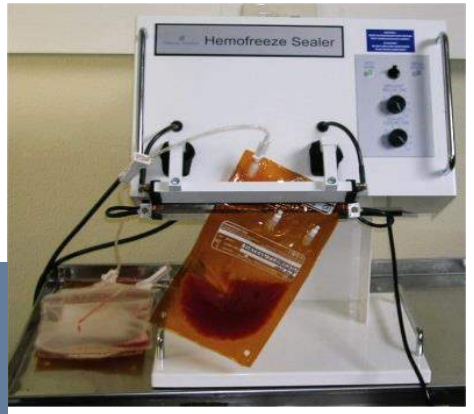
CSE defrosting

- The product (PBSC / BM) should be frozen QUICKLY, in the humidifier with a thermostat at 37 ° C, without leaving the product at room temperature before the infusion.

- Exposure to DMSO after thawing must be MINIMUM to avoid cell death.
- Special attention to cross-contamination during defrosting!







Cryopreservation : devices

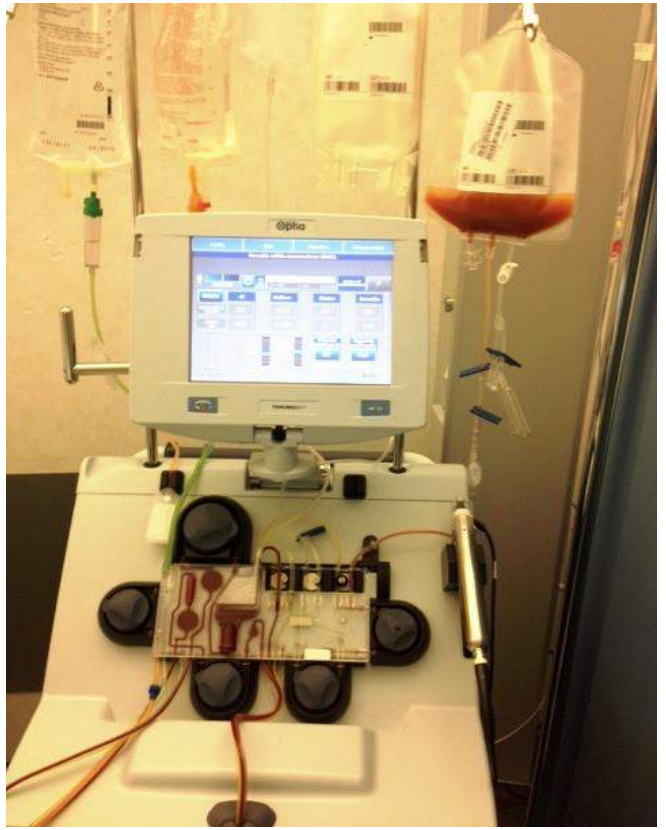
Process Validation

- According to Jacie Standards, the collection, manipulation and clinical use of peripheral blood stem cells must be validated and monitored.
- Each process needs to be validated:

1. environment
2. separators
3. reagents
4. collection
5. labeling
6. transport of biological material

Cell Separator Validation Proccess

- Necessary to exclude isolated or systematic errors in the apheresis procedure.

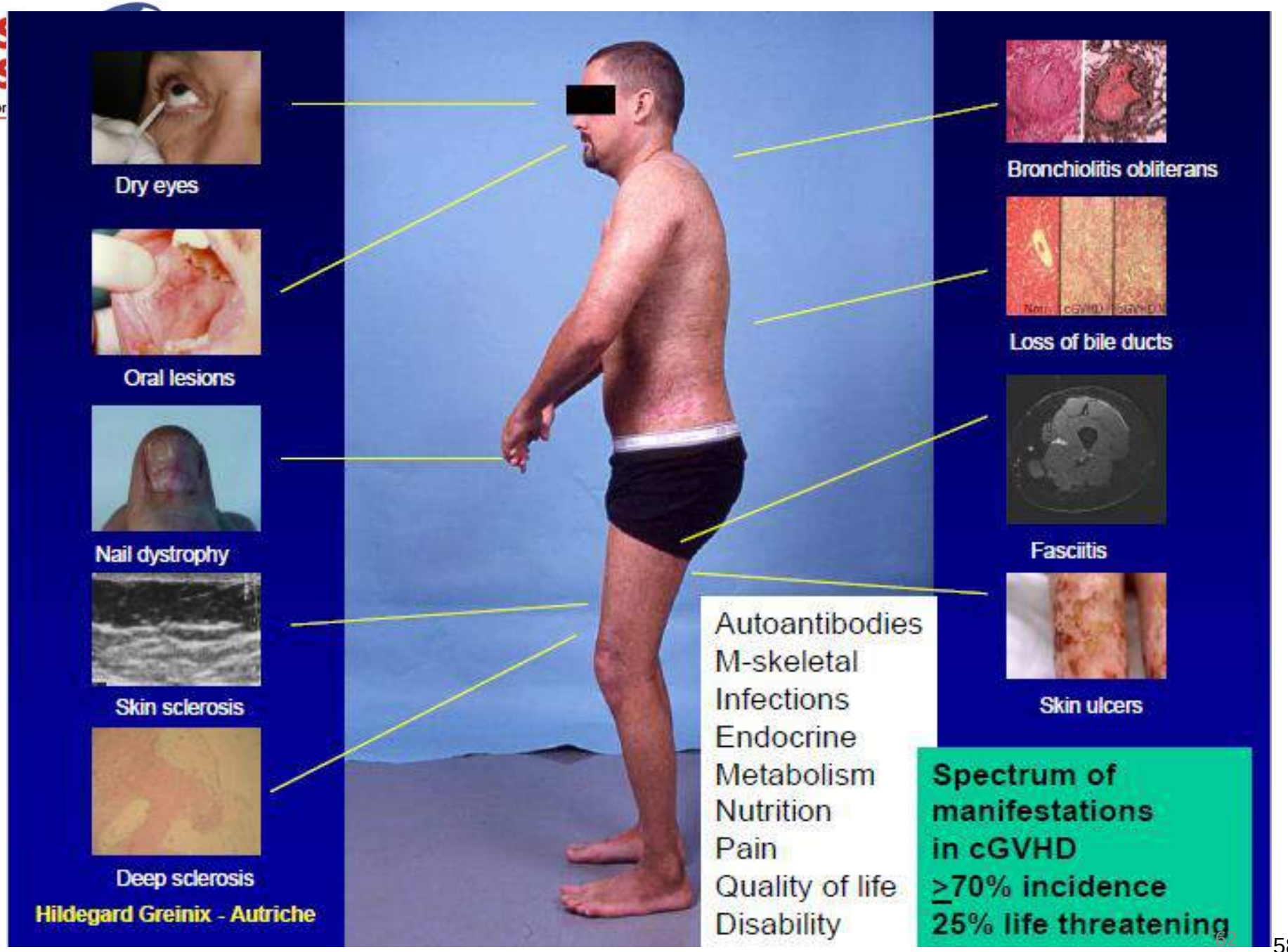


German/Austrian/Swiss Consensus on First-line Treatment of cGVHD

Role of ECP

- Published evidence mainly available on use of ECP in steroid-refractory cGVHD.
- In view of the promising results of ECP with almost no severe side effects, **use of ECP as first-line therapy is justified.**
- Prospective studies with homogeneous patient populations needed.

Hildegard Greinix - Autriche



Different ECP technique

	Line	Flow modality	Flow rate ml/min	8-MOP dosage	Anti coagulation	WBC collected per session	Extra corporeal volume ml
Uvar XTS	ON	Discontinuous	5 – 30	340 ng/ml	Heparin	3 x 10^9	350 – 600 (Ht)
Cellex	ON	Continuous/ Discontinuous	5 – 50	340 ng/ml	Heparin or ACD-A	5 x 10^9	216 dn 266 sn Bisaccia, BjD 2009
Comtec Fresenius	OFF	Continuous	10 – 60	200 ng/ml	ACD-A or ACD-A plus Heparin	4 x 10^9	180
Cobe spectra	OFF	Continuous	10 - 60	200 ng/ml	ACD-A or ACD-A plus Heparin	**7,1 x 109** Garban, Haematologica 2005	Auto-PBS: 170 MNC: 280

General technical aspects

- Lymphocytes > 200 x 103/µl
- PLT > 30.000 x 103/µl
- Hb > 9 g/dl (depending on separator)
- If pts weight < 40 Kg NO discontinuous flow
- If pts weight < 20 Kg priming with whole blood (even with continuous flow separators)
- Evaluate any disseminated infection (bacterial, viral, fungal)
- Evaluate organ failure
- Appropriate venous access (CVC or peripheral veins)

IEO
Istituto Europeo di Oncologia
Divisione di Ematoncologia
Centro di Raccolta (CIC 331)

CENTRO di RACCOLTA
ieo – cic 331

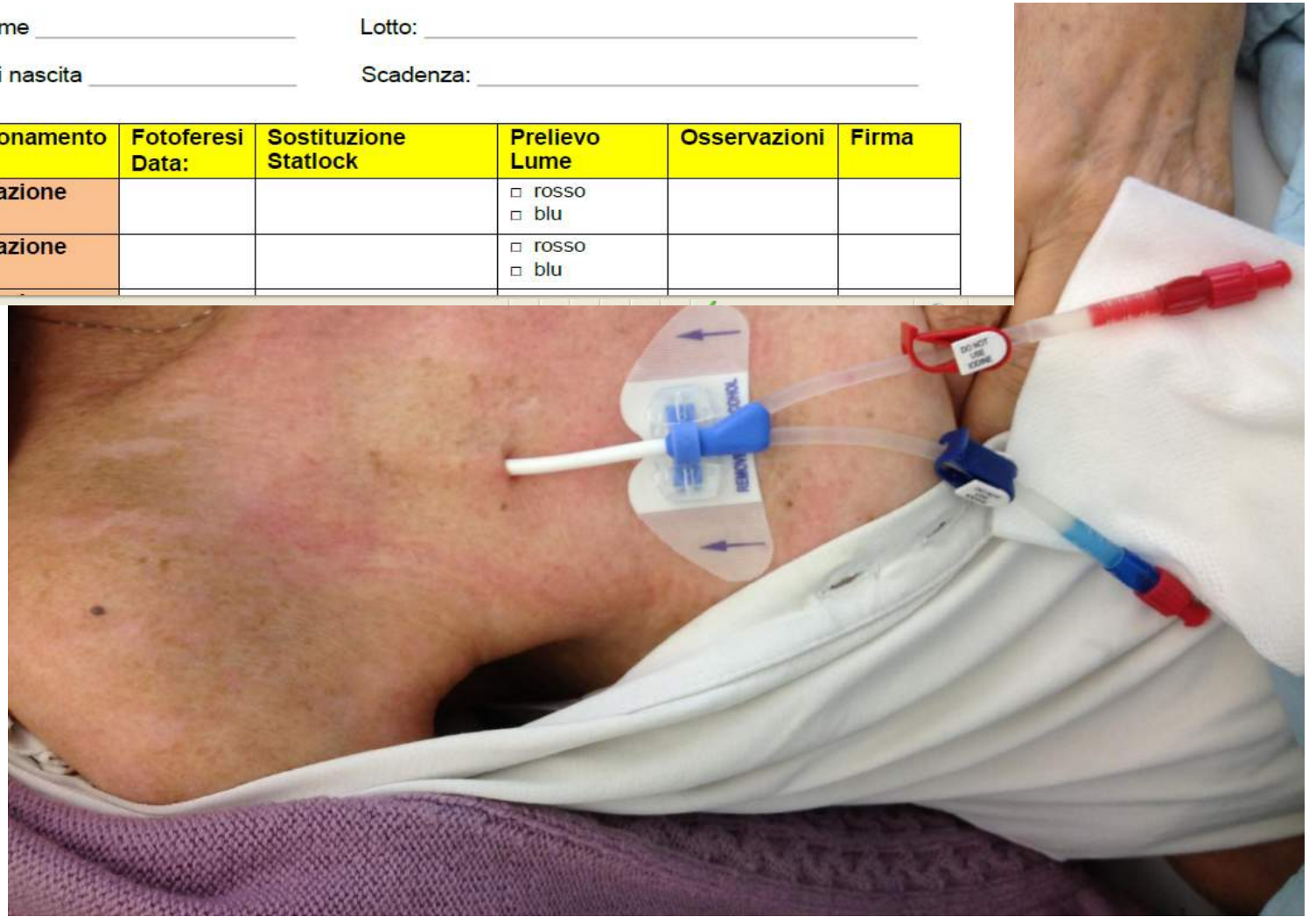
Calendario medicazione catetere tunnelizzato a lungo termine

Nome _____ Modello del catetere: _____

Cognome _____ Lotto: _____

Data di nascita _____ Scadenza: _____

Posizionamento Data:	Fotoferesi Data:	Sostituzione Statlock	Prelievo Lume	Osservazioni	Firma
Medicazione Data:			□ rosso □ blu		
Medicazione Data:			□ rosso □ blu		



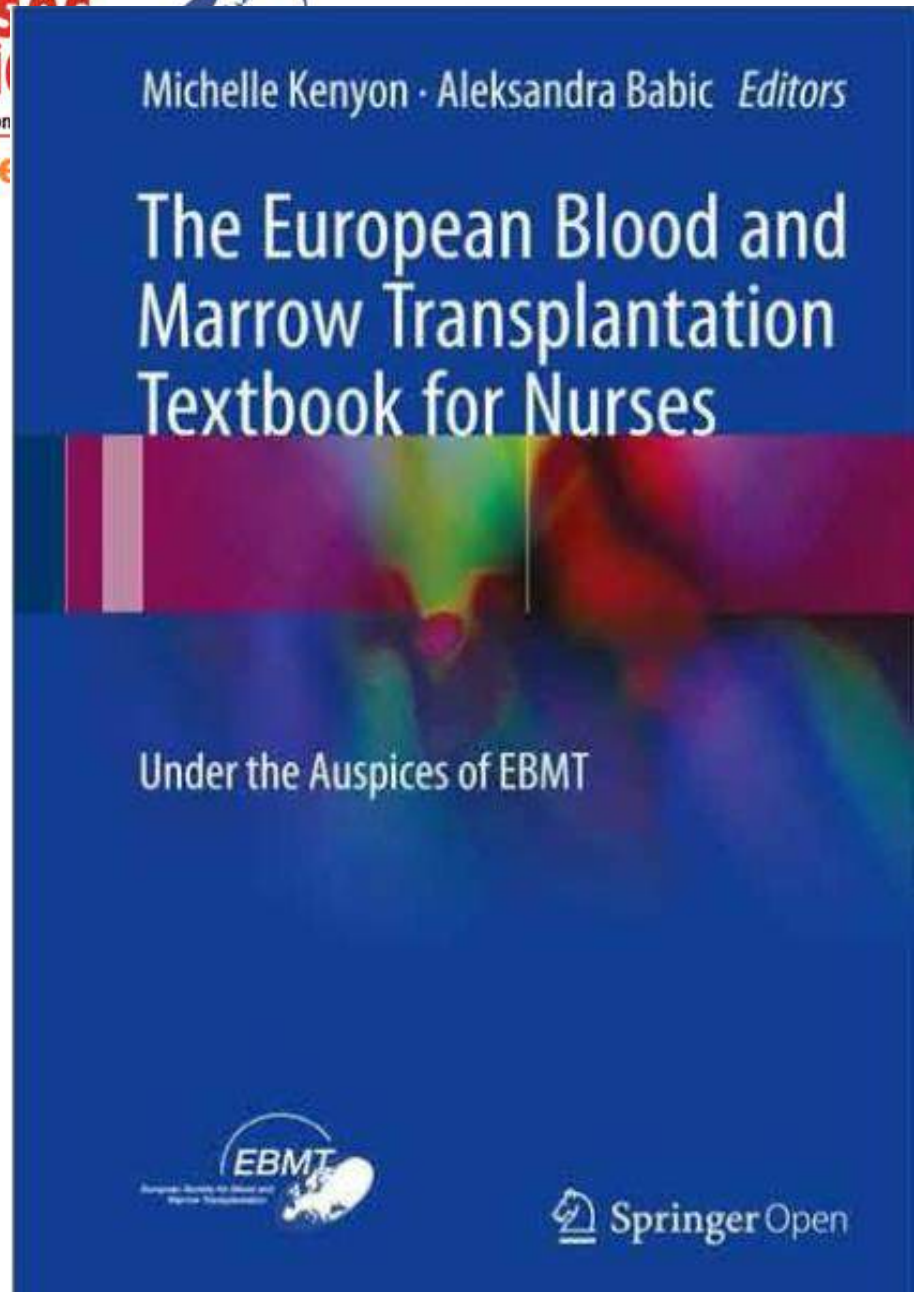
Quality of life data

- Utility data were also derived from published literature. In a retrospective study of 44 children with chronic GVHD, Messina et al. (2003) reported that after treatment with ECP, the patients' quality of life, measured as the median Lansky/Karnofsky score, improved from 60% (range 30-90%) at the start of ECP to 90% (range 60–100%).

(Source: Preference Weights 19982001).

Impact of extracorporeal photopheresis on skin scores and quality of life in patients with steroid-refractory chronic GVHD
Response was assessed after 6 months of treatment using NIH scoring criteria and reduction in immunosuppression. QoL assessments were undertaken at baseline and at 6 months using the chronic GVHD symptom scale (cGVHD SS) and dermatology life quality index (DLQI). An intention-to-treat analysis showed that 19/38 (50%) of patients had a complete or partial response. 27 out of 38 patients completed 6 months of ECP treatment and 70% (19/27) had a complete or partial response. 80%of patients who completed 6 months of ECP treatment had a reduction in immunosuppression dose. 17out of 18 patients (**94%) showed an improvement in scores.**

FL Dignan1,2,3, S Aguilar1, JJ Scarisbrick4, BE Sha



Introduction - HSCT nursing through the ages/ the evolution of the HSCT nurse

1. JACIE & Quality management in HSCT – Implications for Nursing
2. HSCT how does it work?
3. Donor selection
4. Transplant Preparation
5. Cell source and Apheresis
6. Principles of Conditioning Therapy & Cell infusion
7. BMT settings, infections and infection control
8. Transplantation through the generations
9. Early and acute complications and the principles of HSCT Nursing Care
10. Supportive Care of the HSCT recipient
11. Graft versus Host Disease (GvHD)
12. Graft versus Tumour effect
13. Engraftment, Graft failure and rejection
14. Late effects and long term follow-up
15. Improving the patient experience through research and audit

GVHD
Graft versus Host Disease

Marta Canesi, Italy

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

Background & Introduction

GVHD is a significant cause of morbidity and mortality in allogeneic HSCT.

It occurs in 30-50% HLA matched sibling donor transplants and 65-70 % in unrelated donor ones (URD).

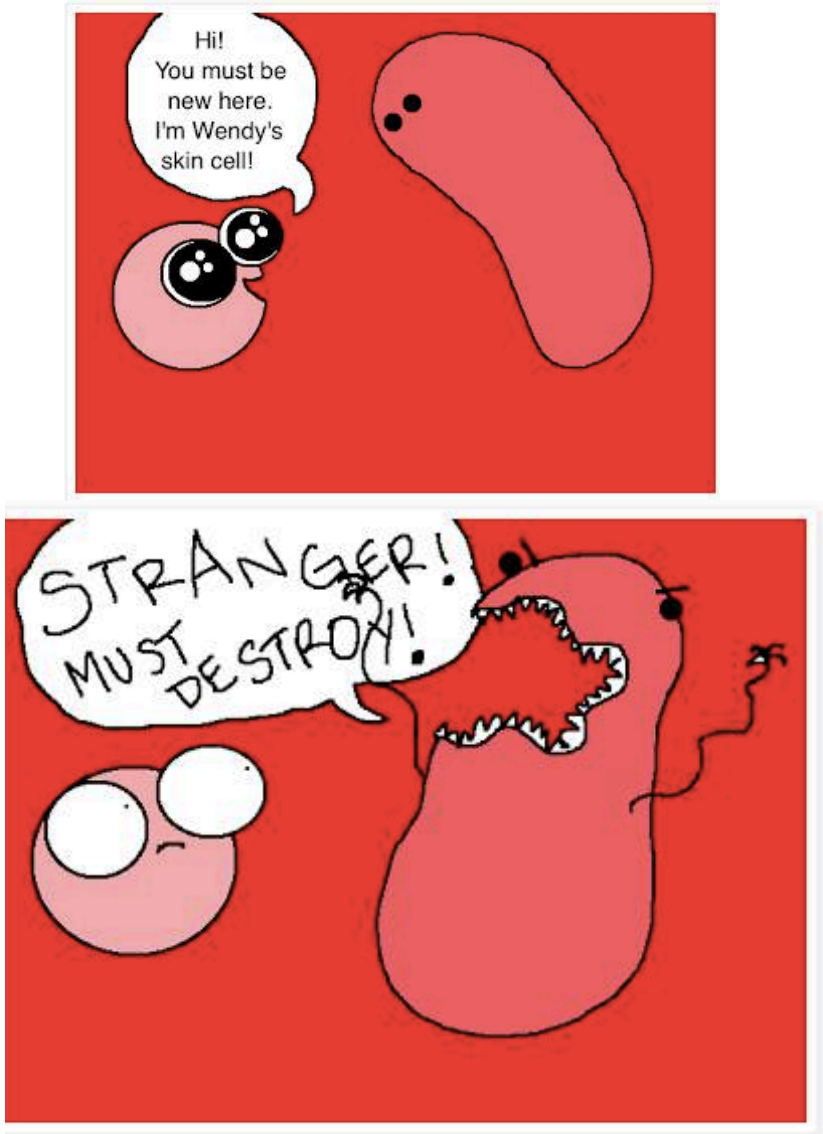
It significantly affects the Quality of Life (QoL).

TISSUE OF THE
PERSON
RECEIVING THE
TRANSPLANT

GRAFT versus HOST DISEASE

SECTION OF TRANSPLANTED
OR DONATED TISSUE
Bone marrow
Peripheral blood cells
Umbelical cord

DONOR TISSUE
ATTACKS THE
RECIPENT BODY CELLS



GvHD is the manifestation of the fight between the **T cells** of the donor and host's immune system.

Allograft

Tissue from a genetically different individual, even between HLA identical individuals (Minor Histocompatibility Antigens)

T cells function

- Protection vs foreign bodies and infections
- Recognise the proteins on the cells as belonging or not belonging to the body

DONOR T- CELLS RECOGNISE THE HOST AS **FOREIGN/NON SELF:**

trigger an immune response between donor and recipient

The greater the difference, the higher the probability of GVHD

3 KEY ELEMENTS

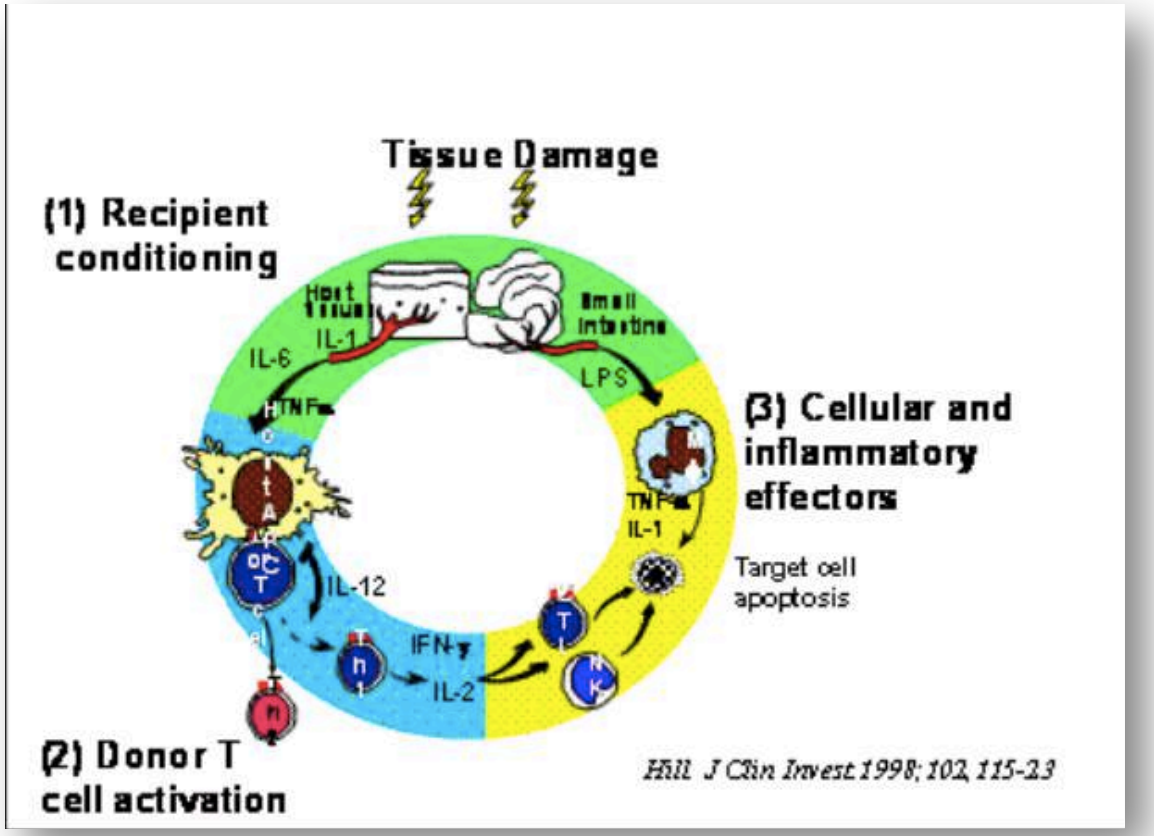
1. Graft must contain **immune cells** (e.g. hematopoietic stem cells)
2. **Inability of the recipient to reject** donor cells (host's immune system is suppressed)
3. Host must be **immunologically different** from the donor (different HLA)

3 PHASE PROCESS

Conditioning regimen (radiotherapy and high dose chemotherapy):
Tissue damage and celll injury and inflammation in the host cells.
Cytokines release (protein mediators)

Host antigen presenting cells (APCs) cause activation
of the donor T cells.

Cytokines and T cells cause cell injury and death (apoptosis)


Tissue Damage
(1) Recipient conditioning
Host tissue
Small intestine
IL-1
IL-6
LPS
HTNF
(3) Cellular and inflammatory effectors
TNF
IL-1
Target cell apoptosis
IL-12
IFN-γ
IL-2
(2) Donor T cell activation
Hill J Clin Invest 1998; 102, 115-23

Risk and influencing factors

DONOR/RECIPIENT RELATED

- HLA mismatch donor/recipient
- Source of stem cells
- Older age of the recipient and the donor
- Sex mismatch (>> female donating to male)
- Female and multipara donor

DISEASE AND CONDITIONING RELATED

- Intensity of conditioning regimen
- Original disease
- TBI in the conditioning
- Original disease (malignant or non malignant)

Assessment and prevention

Recognizing marrow transplant complications early is critical to the health of transplant recipients

- TIMING: every 3 months and when a major change occurs
- It is recommended to score the single organ and the global severity of GVHD
- Assessment with non specific ancillary measures is recommended: Quality of Life score (SF-36, FACT-BMT, CHRIs), performance score (Karnofsky score), grip strenght

Classification

Historically the main classification criteria was the **timing of onset.**

Currently, timing of onset is **insufficient** to distinguish the two.

More attention is paid to **clinical manifestation** rather than temporal onset of symptoms.

Classification (II)

(last update NIH Consensus 2014)

acute GVHD

- classic aGHVD occurring within 100 days after HSCT
- persistent, recurrent or late onset acute GVHD: features of classic aGVHD occurring beyond 100 days post HSCT

in a patient not meeting criteria for the diagnosis of cGVHD

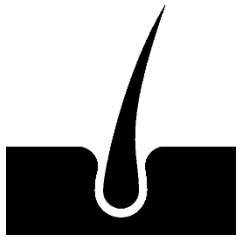
chronic GVHD

- classic cGHVD without features characteristic of aGVHD
- overlap syndrome: presence of one or more aGVHD manifestations in a patient with a diagnosis of cGVHD

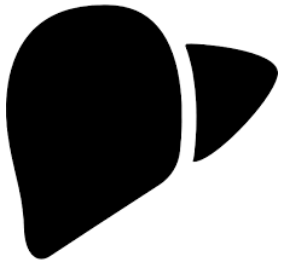
Acute GVHD

35-50% of HSCT recipients will develop aGVHD

The three most affected organs are:



SKIN



LIVER

GI tract

aGVHD grading and staging: *Glucksberg-Seattle criteria*

Stage	Clinical: Skin (Body Surface Area)	Clinical: Liver (Bilirubin Level, mg/100 mL)	Clinical: Gastrointestinal Tract (Volume of Diarrhea, mL/d)
I	Erythematous macules and papules, 25% BSA	2-3	500-1000
II	Erythematous macules and papules, 25%-50% BSA	3-6	1000-1500
III	Erythematous macules and papules (>50% BSA) to generalized erythroderma	6-15	1500-2000
IV	Generalized erythroderma with bullae formation	>15	>2000; Severe abdominal pain with or without ileus

STAGE: 0 to 4 FOR EACH ORGAN

SKIN: Percentage of Body Surface Area involved (%)

LIVER: bilirubin level (lab test)

GI tract: volume of stools

aGVHD grading and staging (II)

Stages → overall GRADE (0 to IV)

Extent of organ involvement			
Stage	**Skin**	**Liver (bilirubin)**	**Gut (stool output per day)**
0	No GVHD rash	<2 mg/dL	<50 mL/day or persistent nausea (child: <10 mL/kg/day)
1	Maculopapular rash <25% BSA	2-3 mg/dL	500-999 mL/day (child: 10-19.9 mL/kg/day) or persistent nausea, vomiting or anorexia, with a positive upper GI biopsy
2	Maculopapular rash 25-50% BSA	3.1-6 mg/dL	1000-1500 mL/day (child: 20-30 mL/kg/day)
3	Maculopapular rash >50% BSA	6.1-15 mg/dL	>1500 mL/day (child: >30 mL/kg/day)
4	Generalized erythema plus bullous formation	>15 mg/dL	Severe abdominal pain with or without ileus
Grade	**Skin**	**Liver (bilirubin)**	**Gut (stool output per day)**
I	Stages 1-2	None	None
II	Stage 3 or	Stage 1 or	Stage 1
III	-	Stage 2-3 or	Stages 2-4
IV	Stage 4 or	Stage 4	-

SKIN + LIVER + GI = overall aGVHD grade

SKIN

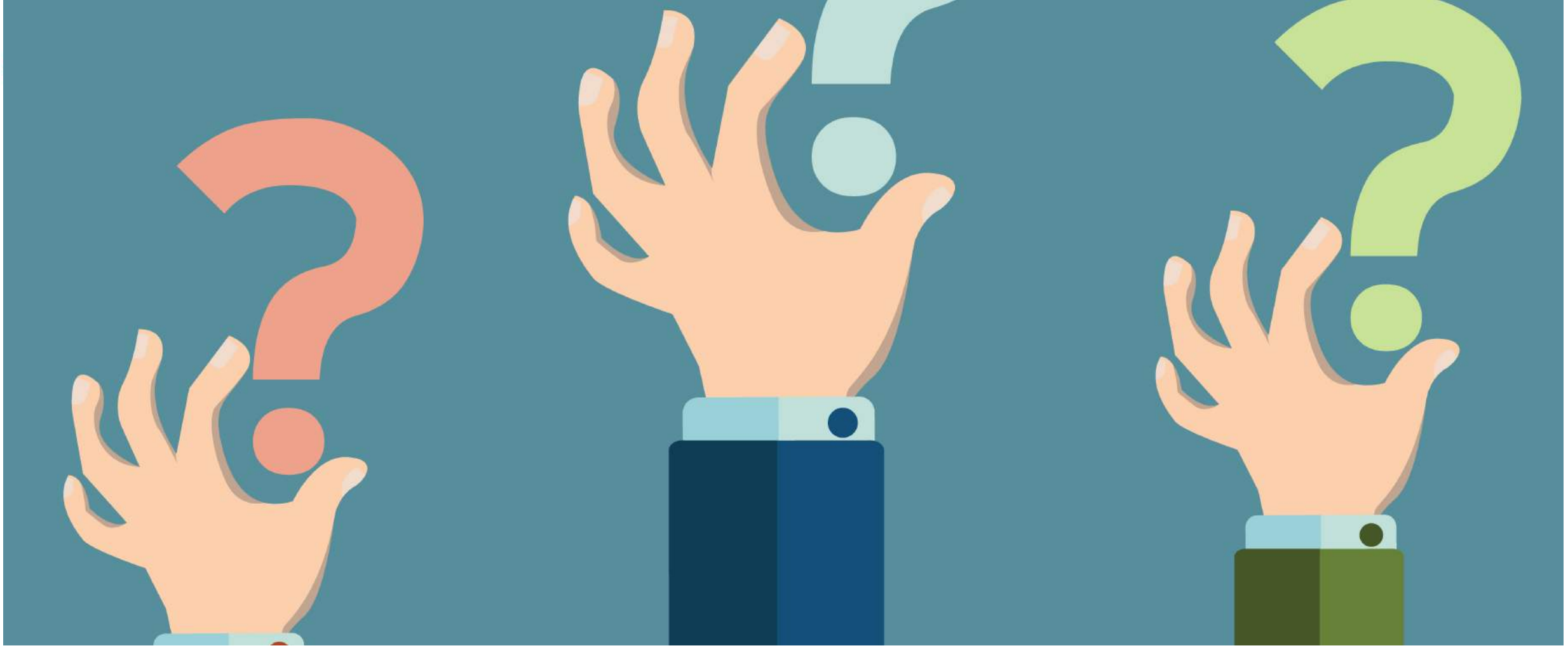
Pruritic and sometimes painful **erythematous-purpuric maculopapular exantema** on the palms, soles, cheeks, neck, ears and upper trunk, preferentially around hair follicles.

As the severity of the GVHD increases, the exantema progresses and can affect the total BSA.

Erythroderma, vescicles, bullae define the most severe form of aGVHD.

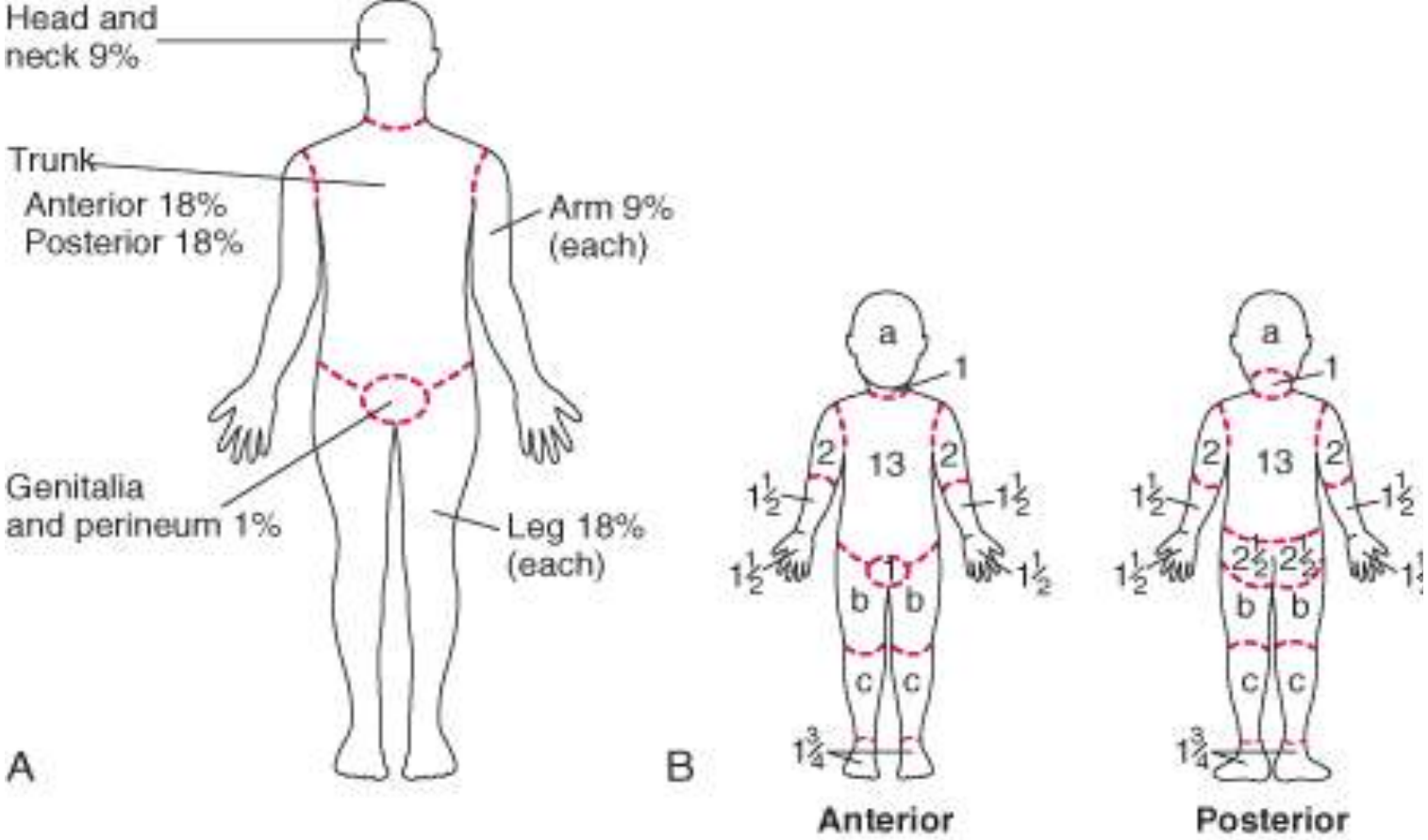
Table 2 Clinical Staging and Histologic Grading of aGVHD by Organ System Involved[26]

	Clinical		
Stage	Skin (Body Surface Area)	Liver (Bilirubin Level, mg/100 mL)	Gastrointestinal Tract (Volume of Diarrhea, mL/d)
I	Erythematous macules and papules, 25% BSA	2-3	500-1000
II	Erythematous macules and papules, 25%-50% BSA	3-6	1000-1500
III	Erythematous macules and papules (>50% BSA) to generalized erythroderma	6-15	1500-2000
IV	Generalized erythroderma with bullae formation	>15	>2000; Severe abdominal pain with or without ileus



How do we calculate the BSA involved?

Rule of 9's



Relative percentage of body surface area (% BSA) affected by growth

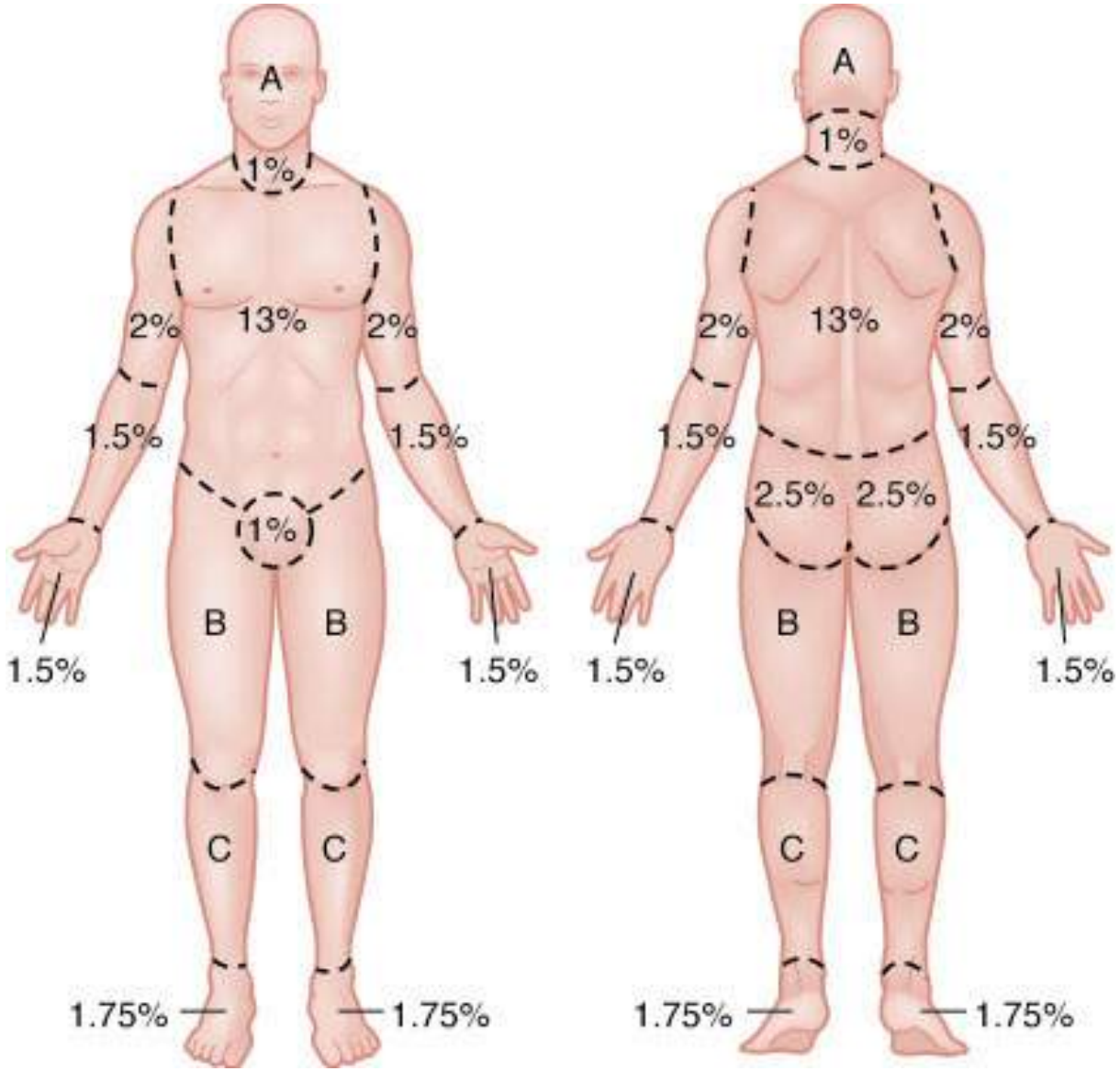
Body Part	Age				
	0 yr	1 yr	5 yr	10 yr	15 yr
a = 1/2 of head	9 1/2	8 1/2	6 1/2	5 1/2	4 1/2
b = 1/2 of 1 thigh	2 3/4	3 1/4	4	4 1/4	4 1/2
c = 1/2 of 1 lower leg	2 1/2	2 1/2	2 3/4	3	3 1/4

LUND-BROWDER DIAGRAM and CHILDREN

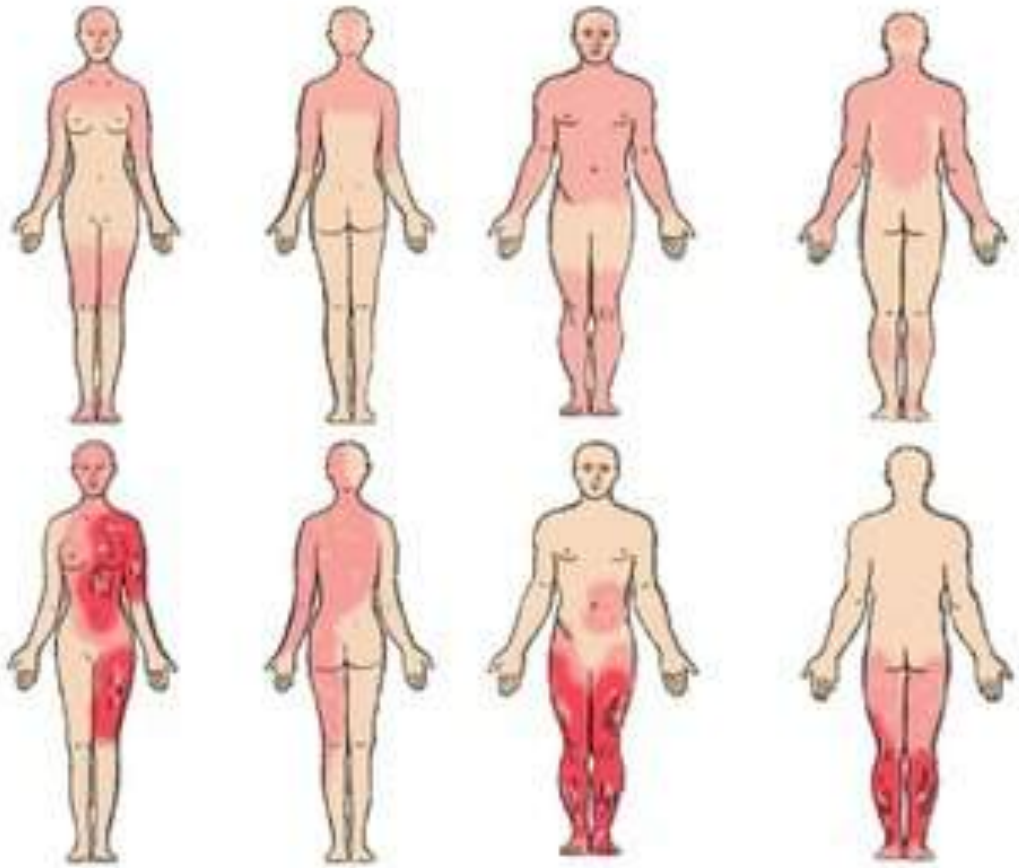
In children, adjust percents because they have proportionally larger heads (up to 20%) and smaller legs (13% in infants) than adults

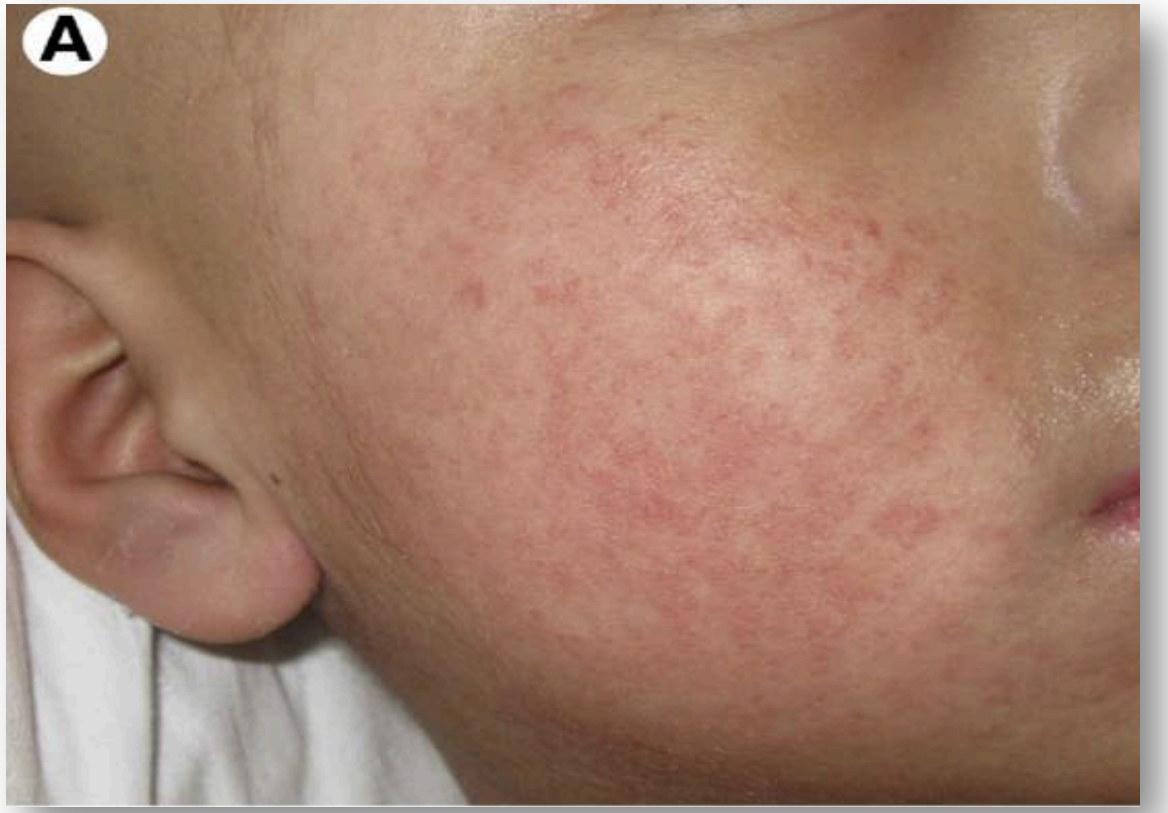
Lund-Browder diagrams improve the accuracy of the % TBSA for children.

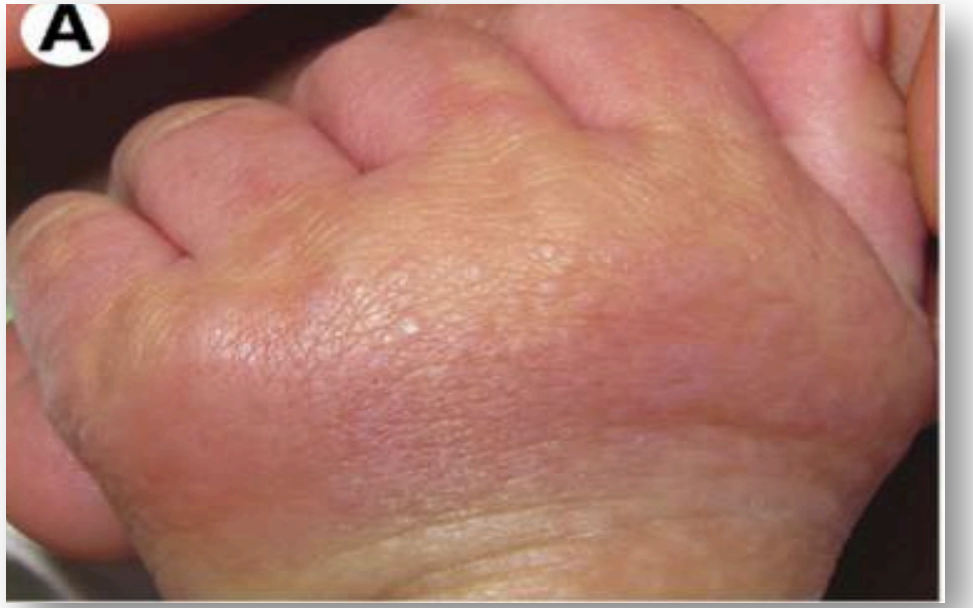
Palmar hand surface is approximately 1% TBSA


A
1%
2%
13%
2%
1.5%
1.5%
1%
B
B
1.5%
1.5%
C
C
1.75%
1.75%
A
1%
2%
13%
2%
1.5%
1.5%
2.5%
2.5%
B
B
1.5%
1.5%
C
C
1.75%
1.75%

Color it!

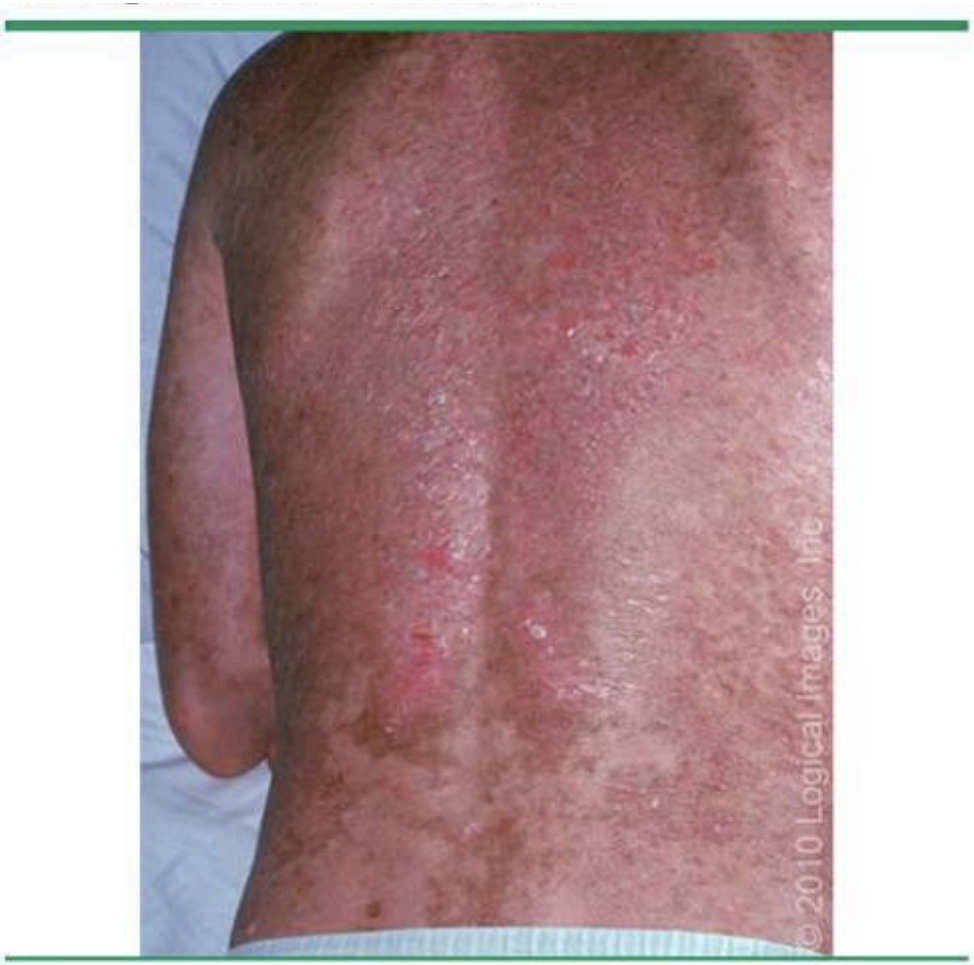






papular rash

Goddard et al. (2010) Clinical Update on GvHD in children



Widespread erythema, desquamation, and postinflammatory hyperpigmentation are evident in this patient with acute graft-versus-host disease.

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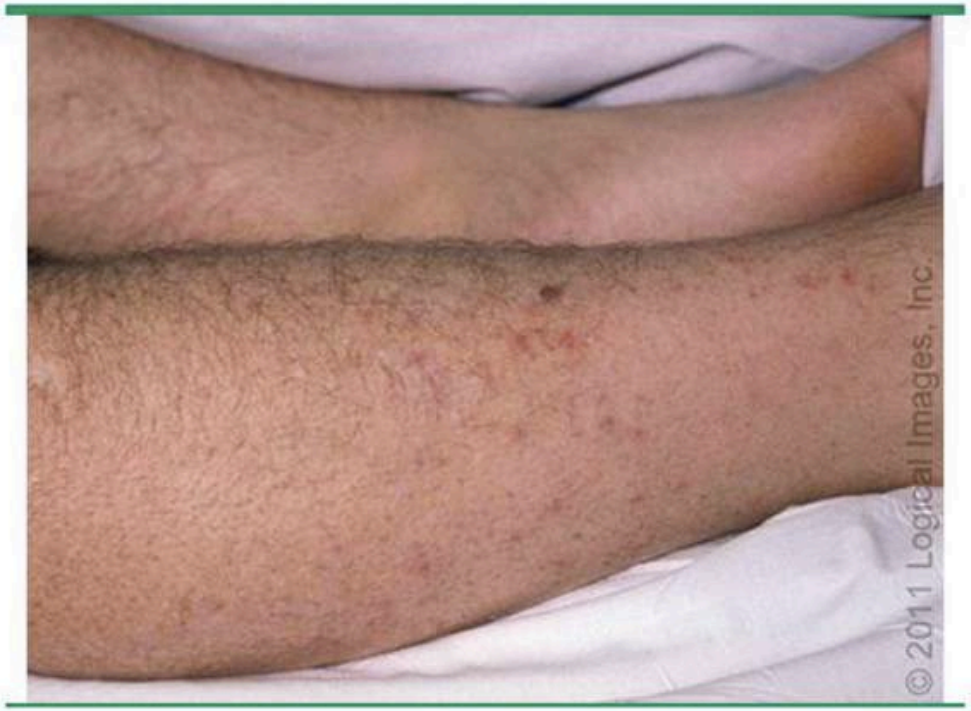
UpToDate®

Nurses Frontiers
www.edu-nursesnofrontiers.com
moodle

EBMT
European Society
for Blood and Marrow Transplantation

Acute graft-versus-host disease



Small, erythematous, follicularly-based macules and papules are present on the distal lower extremities in this patient with acute graft-versus-host disease.

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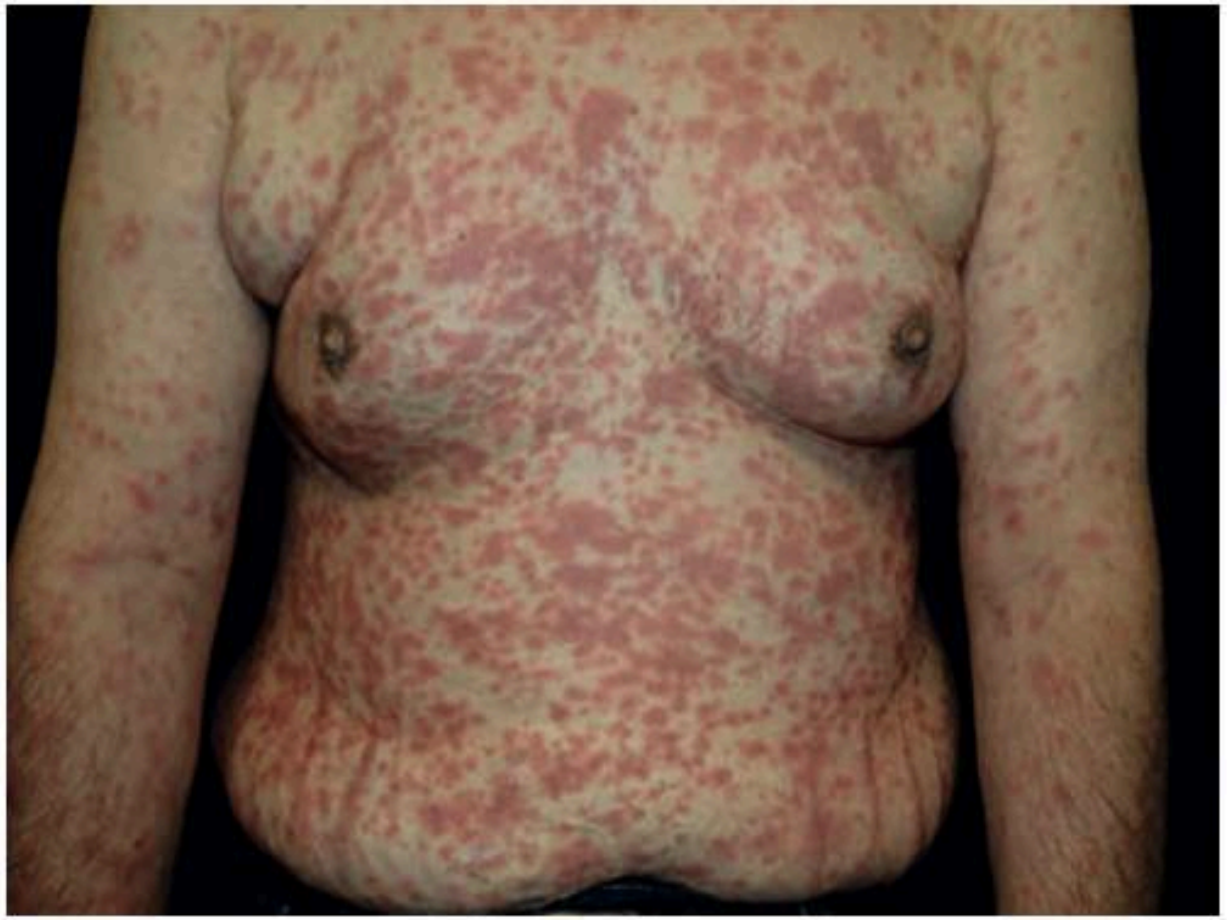
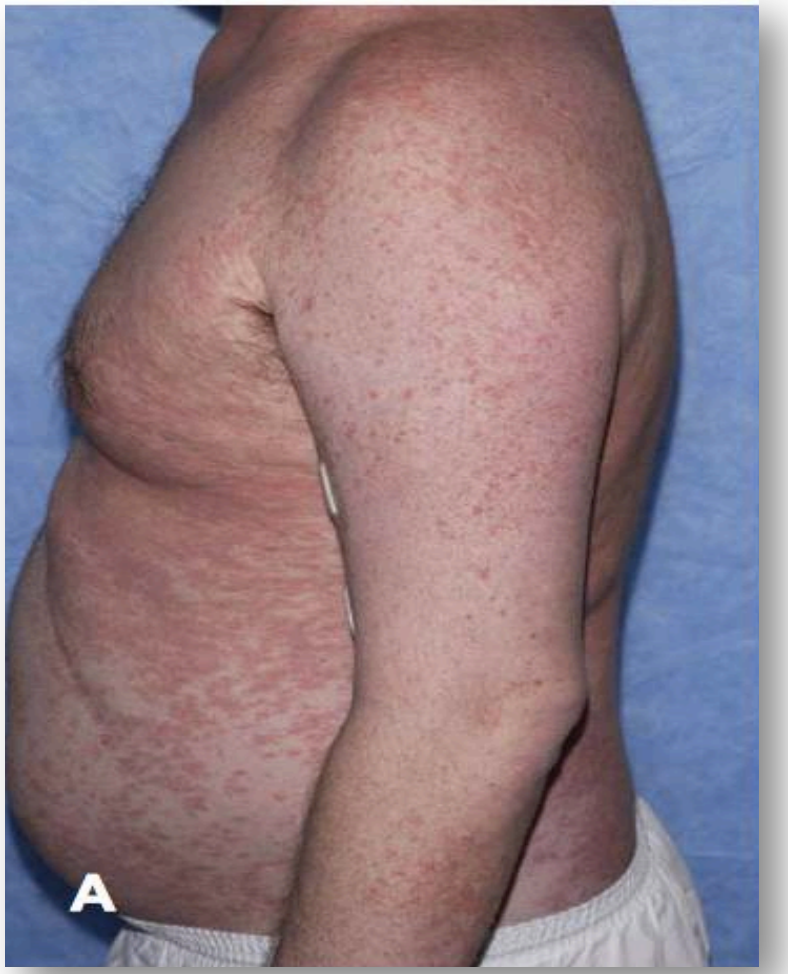
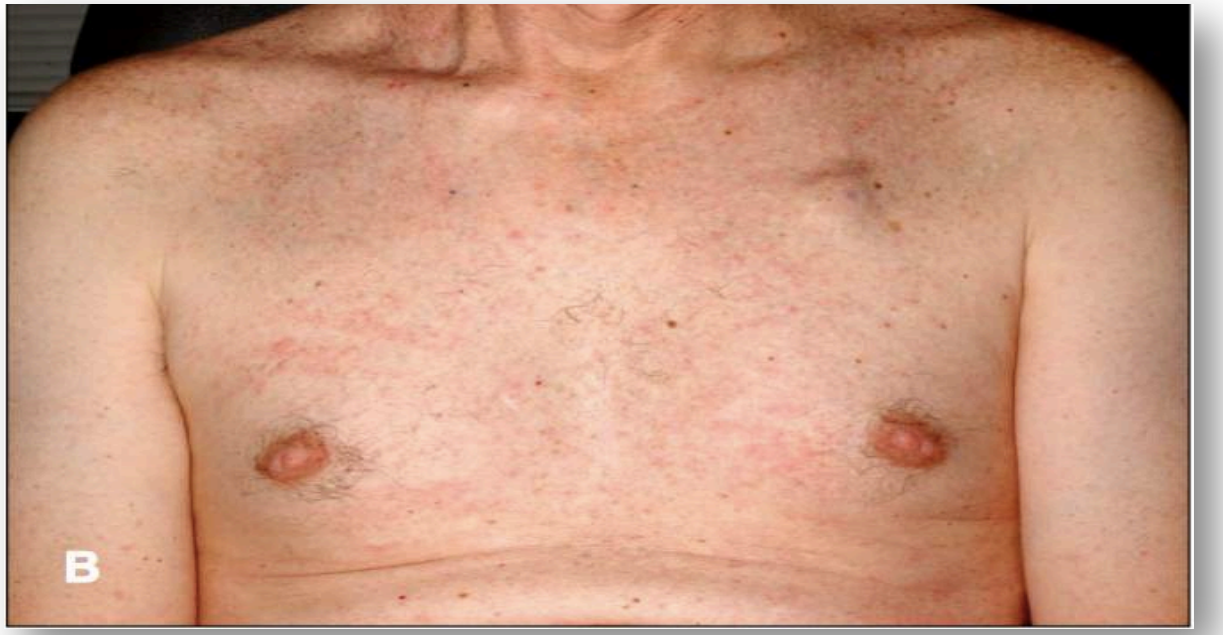


FIGURE 3: Clinical manifestations of cutaneous GVHD. Patient with GVHD grade 3, maculopapular erythematous rash affecting the anterior portion of thorax and extremities

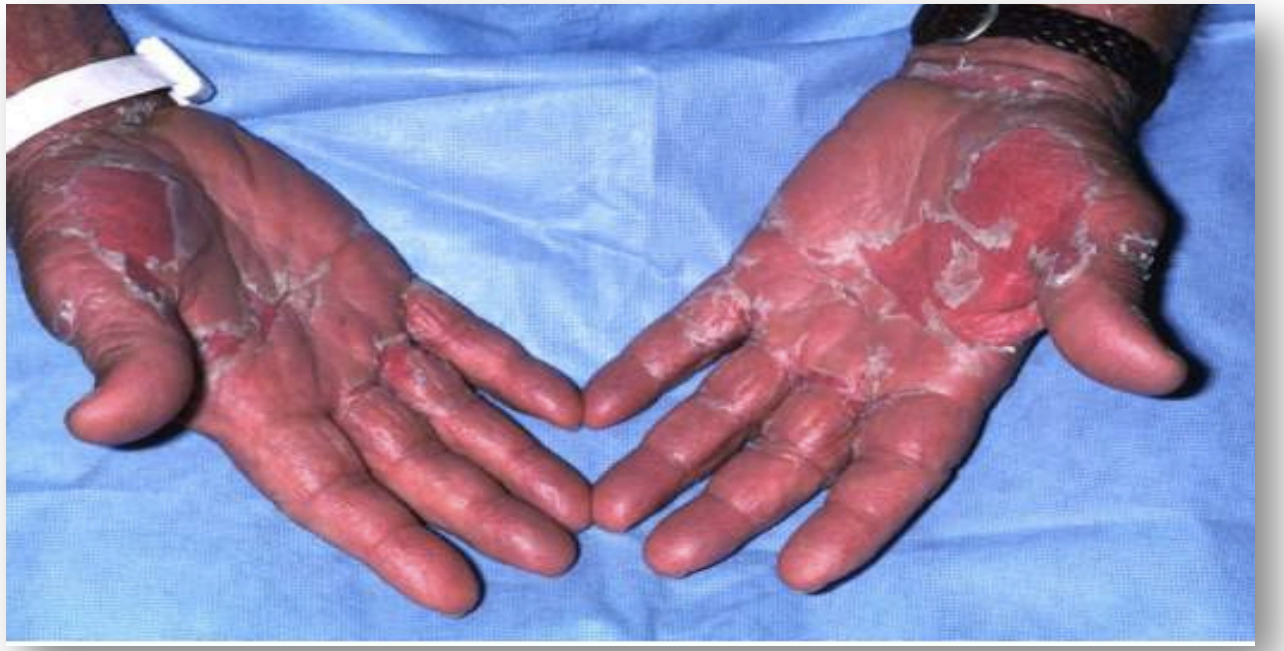


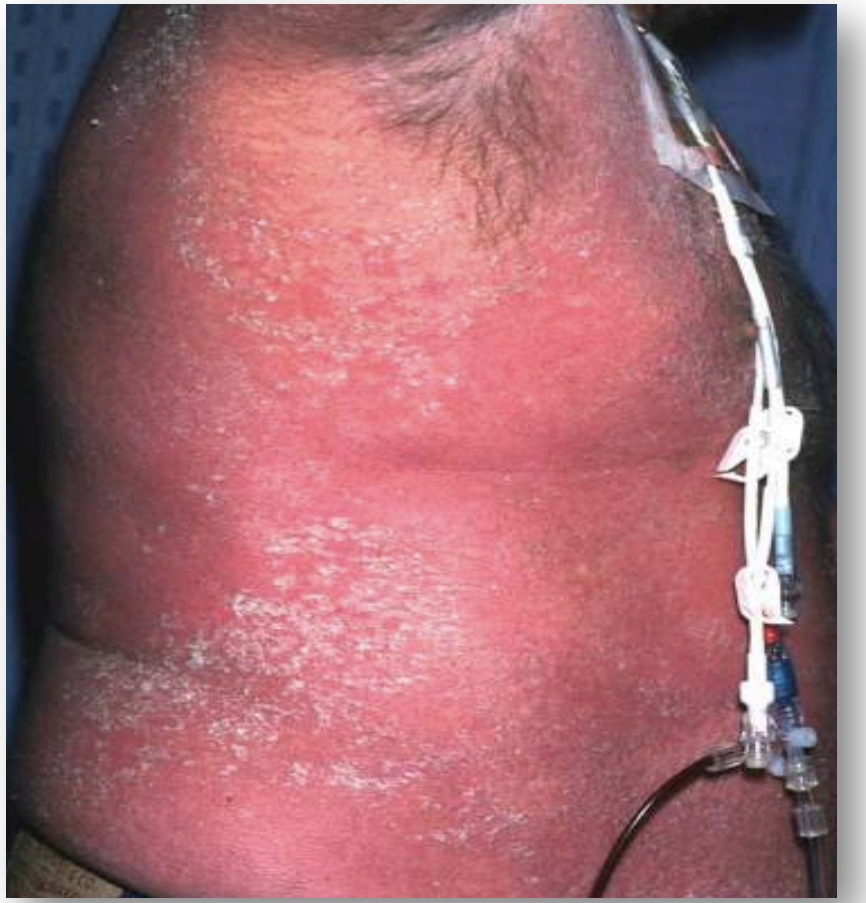
confluent rash



morbilliform

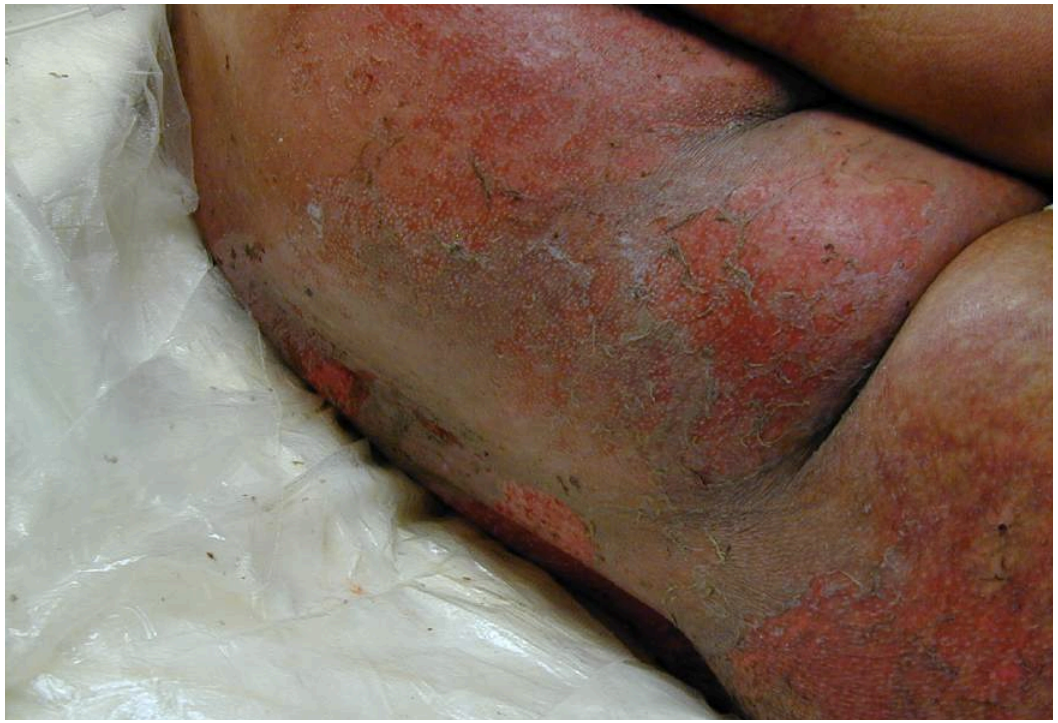
Turner, Cowen (n.n) GvHD skin Atlas

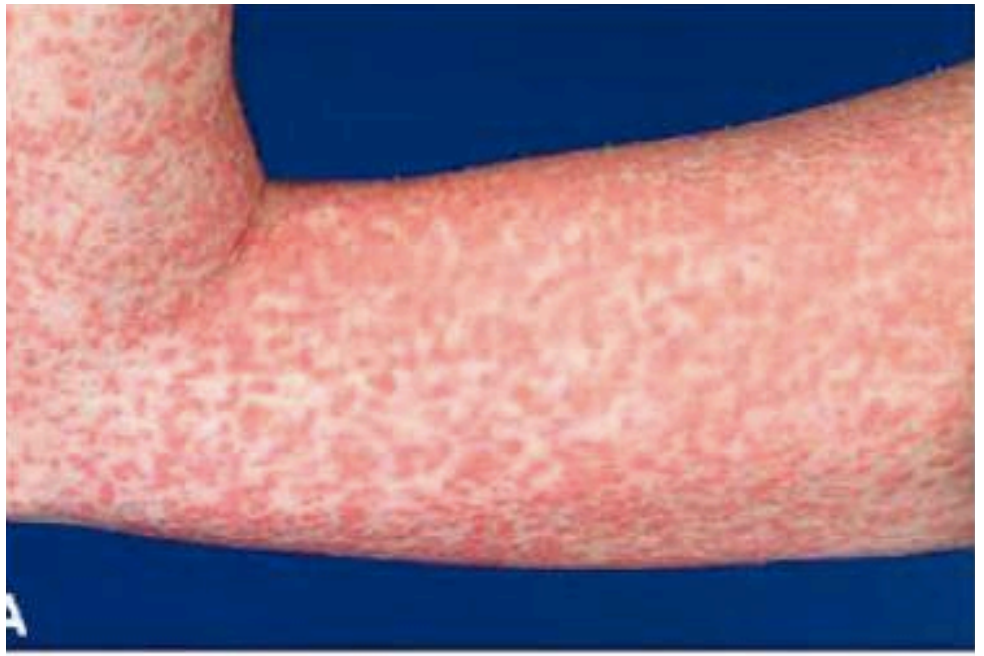




erythroderma and desquamation

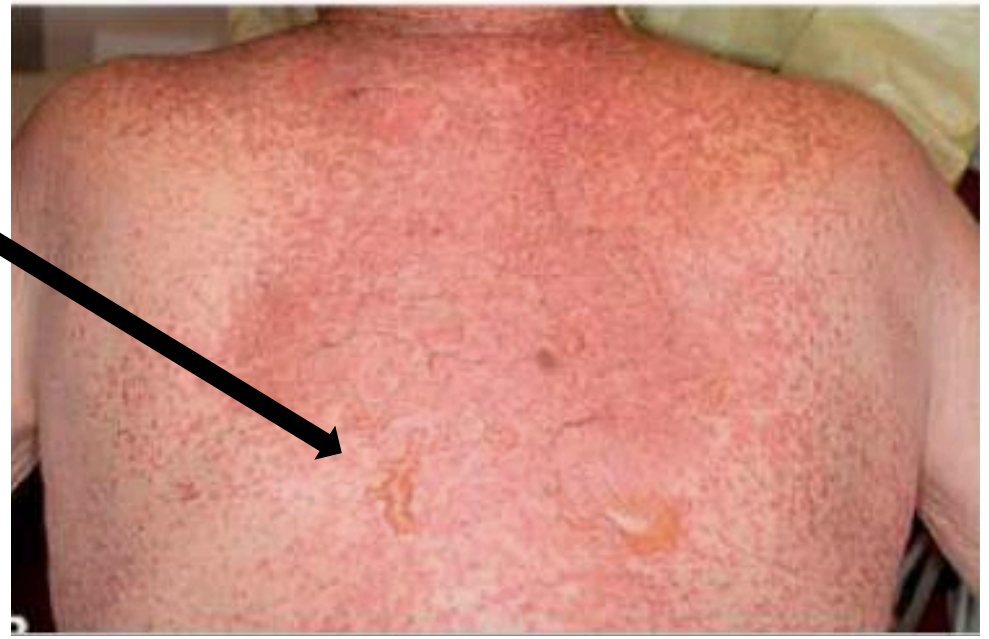
Turner, Cowen (n.n) GvHD skin Atlas





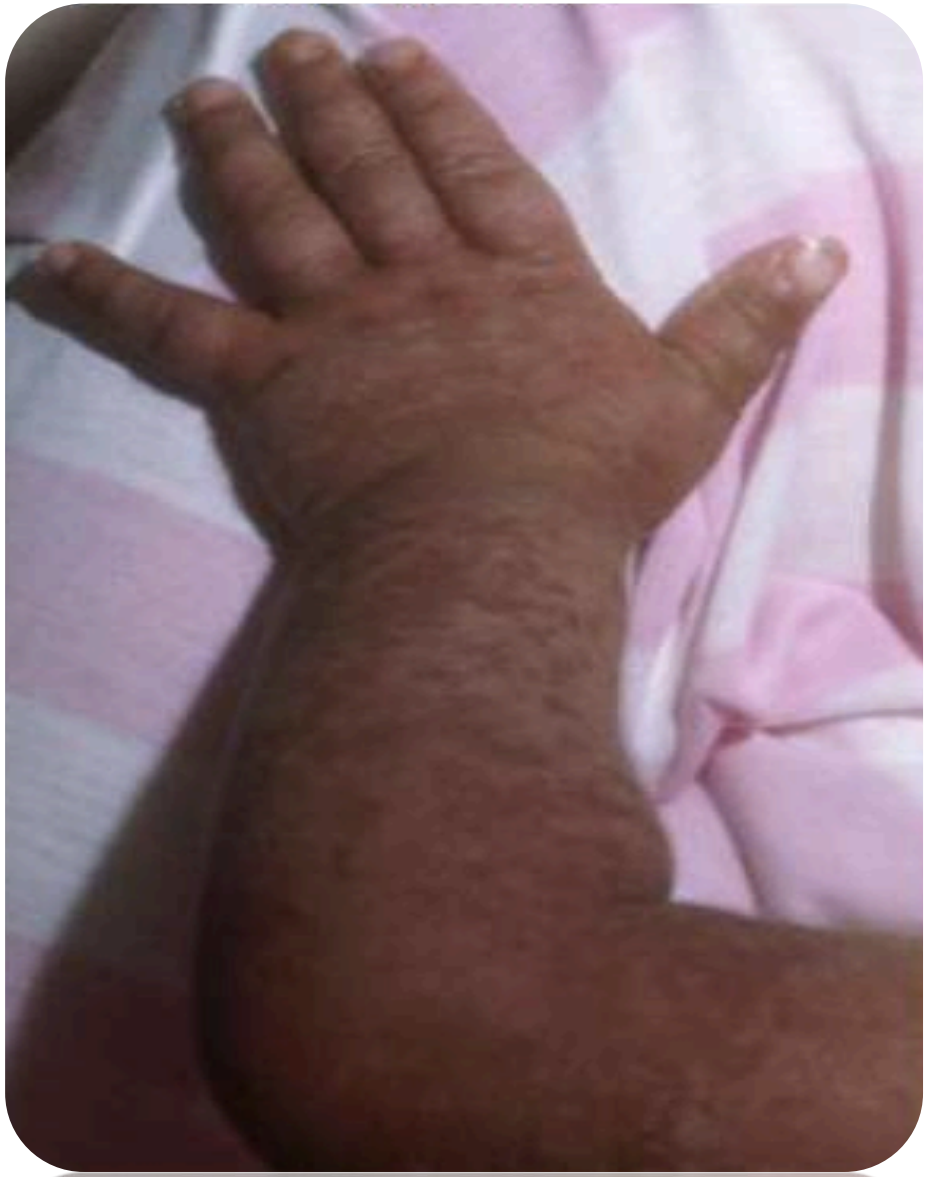
Erythematous maculopapular rash (morbilliform eruption) – **Nikolsky sign**

(skin finding in which the top layers of the skin slip away from the lower layers when rubbed)



www.medscape.com

blisters and bullae



Scheinfeld et al. (2015) Dermatologic manifestation of GvHD

Table 3

Differential diagnosis of aGVHD

AGVHD Manifestation	Differential Diagnosis
Rash	Drug Reaction
	Allergic Reaction
	Infection
	Regimen-related toxicity

Carpenter, MacMillan (2010) Management of acute GvHD in children

LIVER

ic Grading of aGVHD by
Clinical
Liver (Bilirubin Level, mg/100 mL)
2-3
3-6
6-15
>15

- Liver GVHD is graded according to the bilirubin level.
- Typically presents with elevated total bilirubine or/and alkalike phosphatase.
- Diagnosis is clinical judgment. Liver biopsy can clarify.

Differential diagnosis: VOD, infection, drug induced, cholelithiasis or other liver problems.

GI Tract

Gastrointestinal Tract (Volume of Diarrhea, mL/d)
500-1000
1000-1500
1500-2000
>2000; Severe abdominal pain with or without ileus

- It is graded according to the daily volume of the stools
- It can affet the gastric or <u>esophageal tissue (stenosis)</u>
- Usually it is associated with: nausea, anorexia, abdominal pain.
- <u>Stools characteristics:</u> watery, secretory diarrhea. Severe cases: bloody diarrhea, containing mucosa.
- Biopsy can confirm the clinical diagnosis

Risk of severe electrolyte abnormalities due to fluid loss (damaged skin, diarrhea) and possibly associated liver disfunction.

aGVHD treatment

Grade II and above: systemic treatment

Steroids remain the best and first-line therapy

Mechanism of action:
suppression of cytokines.
Antinflammatory response.

Side effects
Hyperglicemia
Hypertension
Osteonecrosis
Higher risk of infections

Organs and their response to steroids:
SKIN: 40%
LIVER: 15-35%
GI TRACT: 45%.

cGVHD

- cGVHD is the most common complication after HSCT : up to 80% of patients.
- 50% of patients with aGVHD will develop cGVHD
- Clinical manifestations of cGVHD often mimic those of autoimmune disorders
- Prevalence and severity are increasing over the years:
    - Stem cells source: PBSC
    - Older recipients
    - Scientific progress in treating and managing patients and complications post allo-HSCT

Children do better than adults

INCIDENCE

27-28%

Growing because of PBSC as stem cells source and URD

Table 3 Bone marrow transplant (BMT) recipient health complications.[4,8,10] The long-term health complications children face post BMT

Health complication	Percent of survivors afflicted
Immunodeficiency	>70
Renal dysfunction	>50
Cataracts	>20
Chronic graft versus host disease	>20
Endocrine dysfunction	>20
Infertility	>20
Delayed sexual development	>20
Oral and dental problems	>20
Psychosocial stress	>10
Secondary malignant neoplasms	>10
Cognitive disorders	>10
Avascular necrosis	>10
Respiratory dysfunction	>10

Children with **non malignant diseases** have reduced risk of developing cGVHD because they do not benefit from GVHD, not needing any GRAFT VERSUS TUMOR effect: stronger prophylaxis and less preparative conditioning regimens.

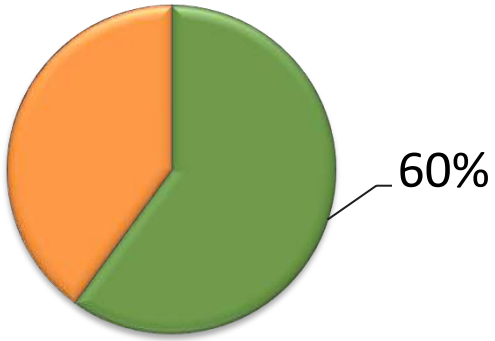
Zecca et al. (2002), Jacobshon D. (2010)

cGVHD and children

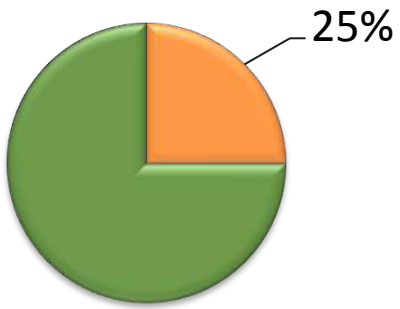
*Chronic GVHD is of major importance in children, especially since they have **years to live** following the complications of cGVHD and its therapy*

(Jacobsohn, D.A., 2010)

1 chronic disease



1 severe complication or life threatening disease



cGVHD (II)

DIAGNOSIS

1.One **diagnostic** manifestation of cGVHD or

2.At least one **distinctive** manifestation + a pertinent biopsy, lab test or other test, evaluation by a specialist or radiographic imaging showing cGVHD in the same or another organ

Drug reaction, infection, recurrent or new malignancies must be excluded. Features should also differ from aGVHD manifestations (dermatitis, enteritis, cholestatic liver manifestation)

cGVHD grading *(NIH score)*

Clinical score to describe how affected the patient is, considering his/her inability to **perform the activity of daily living** (ADL)

Organs and sites to be scored include:

1. Skin
2. Mouth
3. Eyes
4. GI tract
5. Liver
6. Lungs
7. Joint and fascia
8. Genital tract

Score 0 to 3, each organ

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
EYES *Keratoconjunctivitis sicca (KCS) confirmed by ophthalmologist:* **Yes** **No** **Not examined**	No symptoms	Mild dry eye symptoms not affecting ADL (requirement of lubricant eye drops ≤ 3 x per day)	Moderate dry eye symptoms partially affecting ADL (requiring lubricant eye drops > 3 x per day or punctal plugs), **WITHOUT** new vision impairment due to KCS	Severe dry eye symptoms significantly affecting ADL (special eyeware to relieve pain) **OR** unable to work because of ocular symptoms **OR** loss of vision due to KCS

(Jagasia et al, 2015; NIH 2014)

NIH Global Severity of cGVHD

MILD

SEVERE

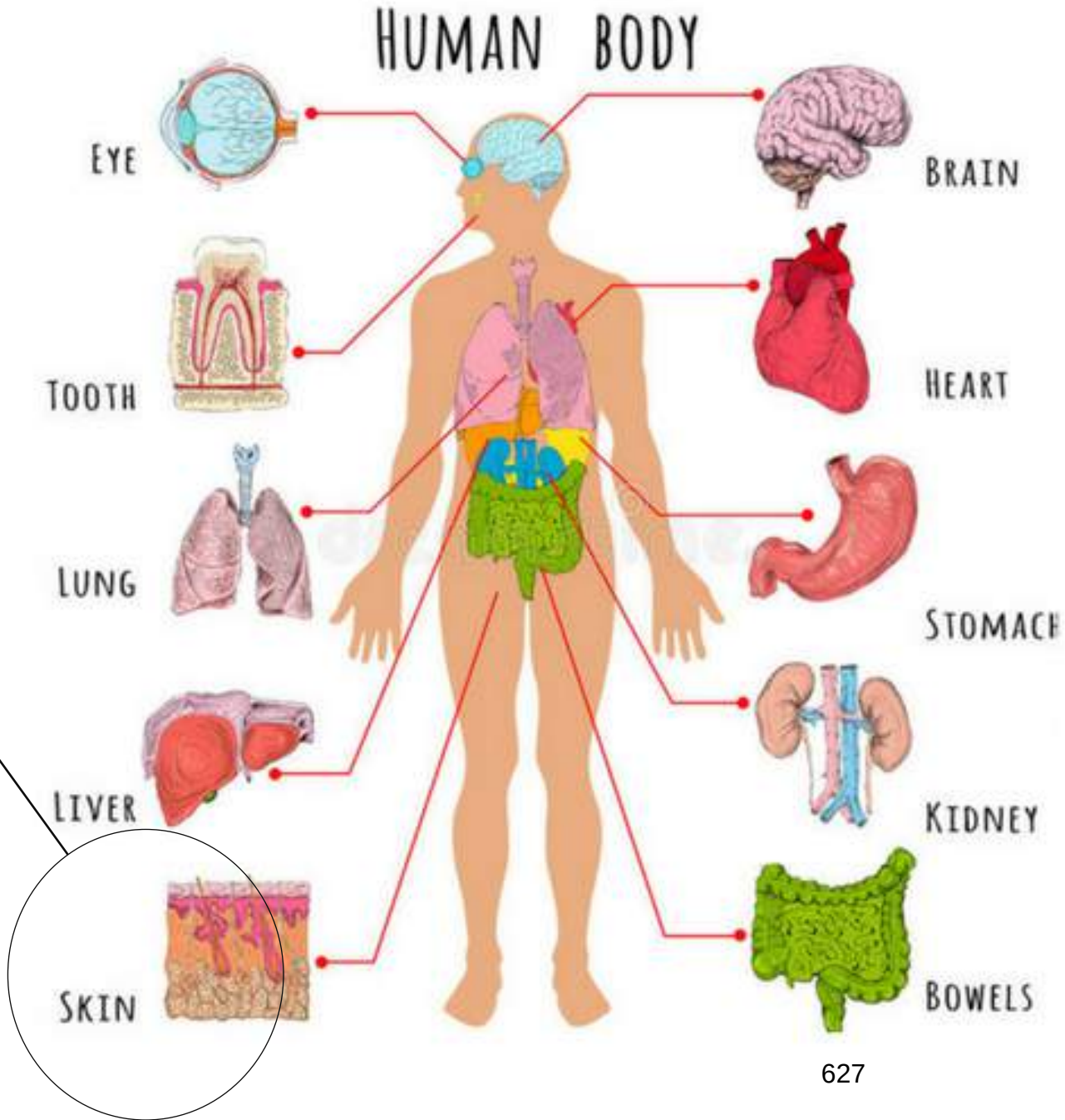
MODERATE

Mild chronic GvHD
1 or 2 organs involved (not lung) *plus*
Score in involved organs 1 *plus*
Lung score 0
Moderate chronic GvHD
3 or more organs involved *plus*
Score of 1 in each organ
OR
Atleast 1 organ (not lung) with a score of 2
OR
Lung score 1
Severe chronic GvHD
1 organ with a score of 3
OR
Lung score of 2 or 3
Key points
1. In skin: Higher of the two scores to be used for calculating global severity.
2. In lung: FEV1 is used instead of clinical score for calculating global severity.
3. If a non-GvHD documented cause unequivocally explains the entire organ abnormality, then the organ is not scored for global severity. If the abnormality is thought to be multifactorial, it is scored without attribution from non-GvHD causes.

SKIN

Most frequently affected organ.

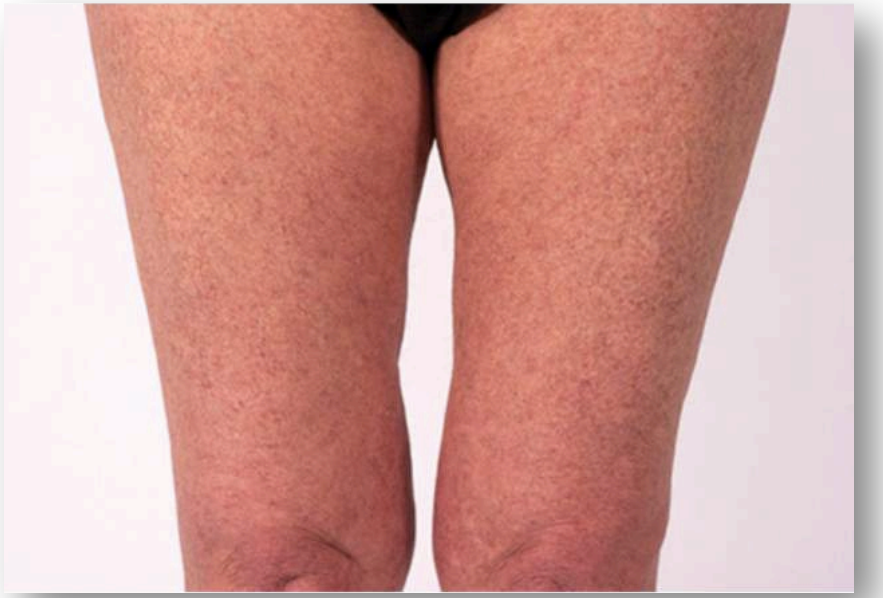
<u>Features:</u> poikiloderma, lichen planus-like superficial sclerotic features or lichen sclerosus-like lesions.



What to do?

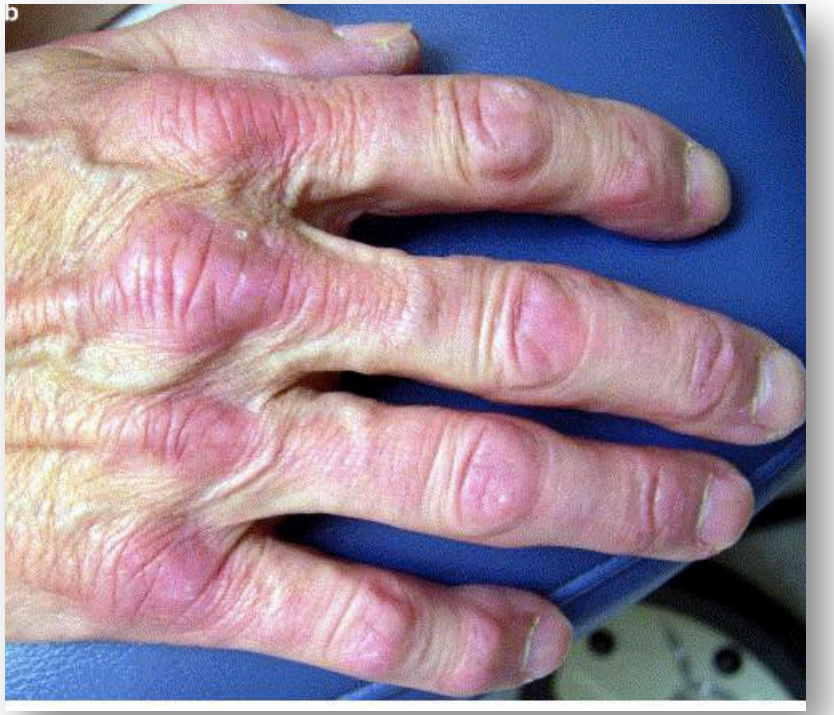
Complete visual examination of the skin with particular attention to pigmentary changes, rashes, textural changes, tightness, areas of thickening or skin breakdown, ulcers or erosions.

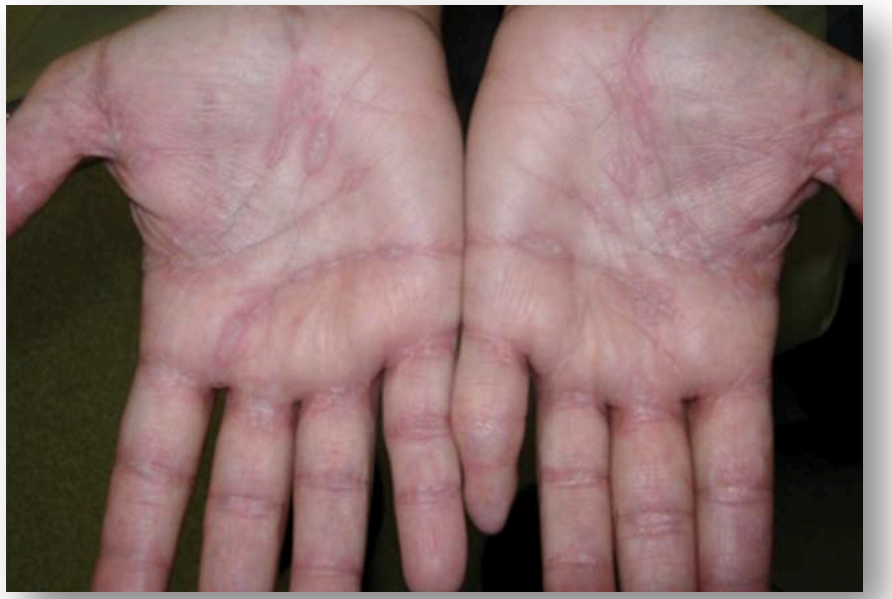
Palpation for areas of sclerosis or fasciitis.



Poikiloderma

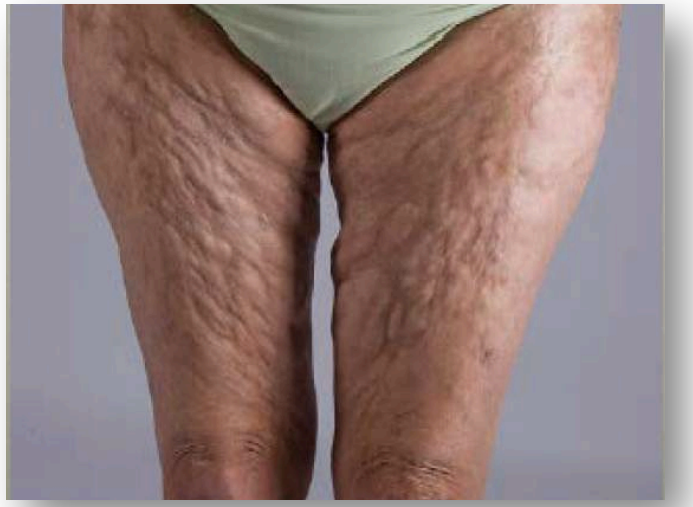
Atrophic and pigmentary changes and teleangectasia

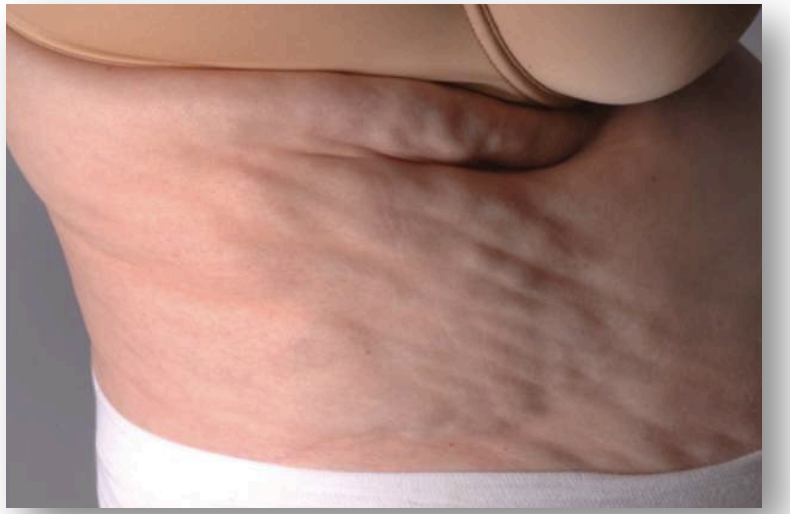


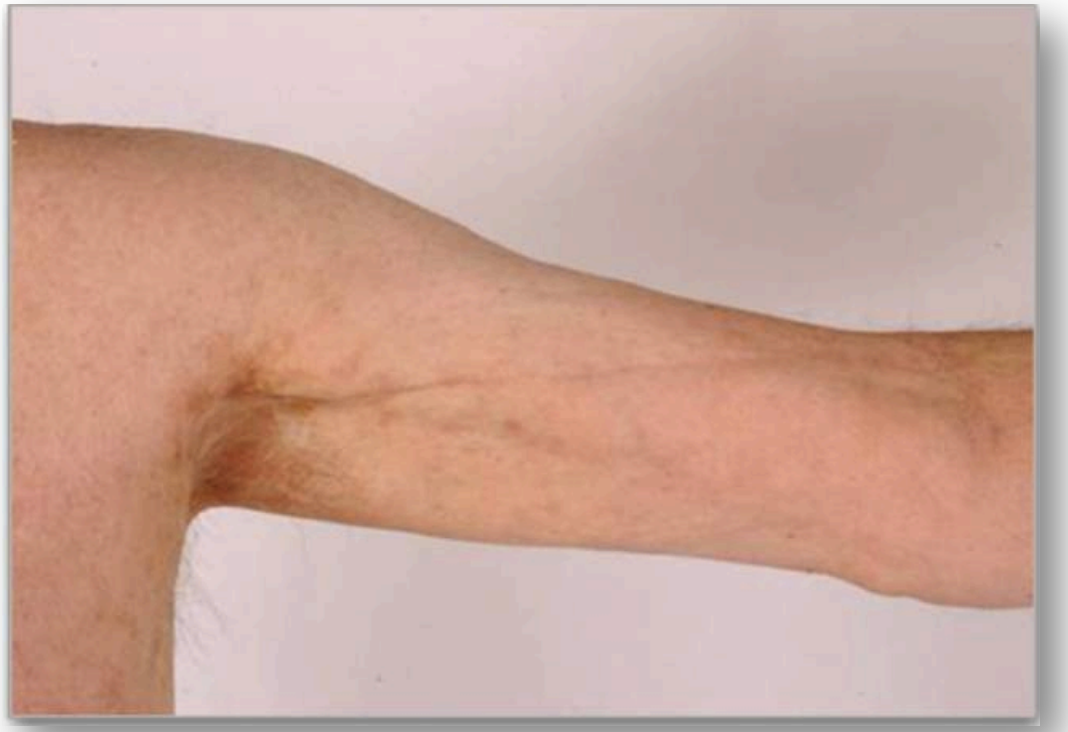


Liken planus-like features

Erythematous/violaceous flat-topped papules or plaques with or without surface reticulations ora silvery/shiny appearance

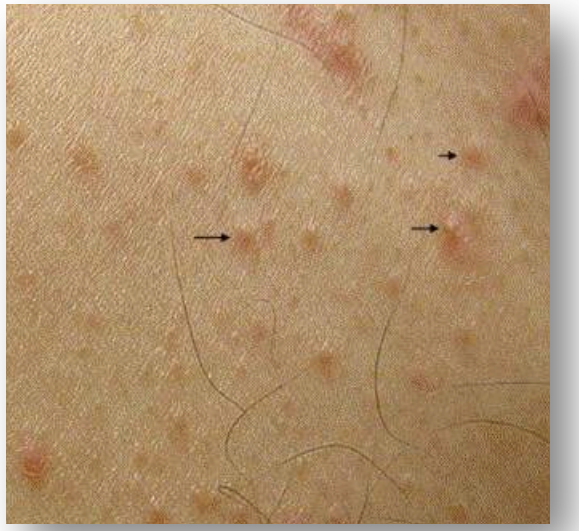




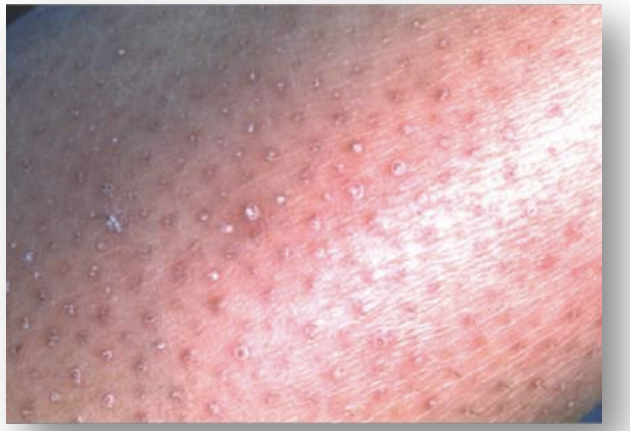


Sclerotic features

Smooth, waxy, indurated, thickened, tight skin and soft tissues caused by deep and diffuse sclerosis over a wide area.

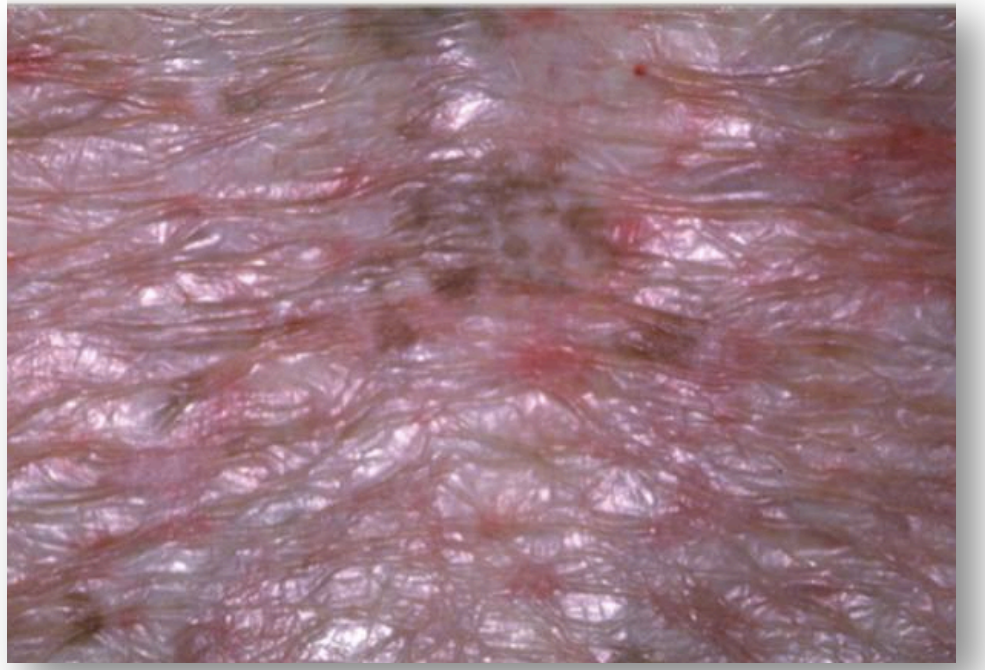


EARLY
STAGE



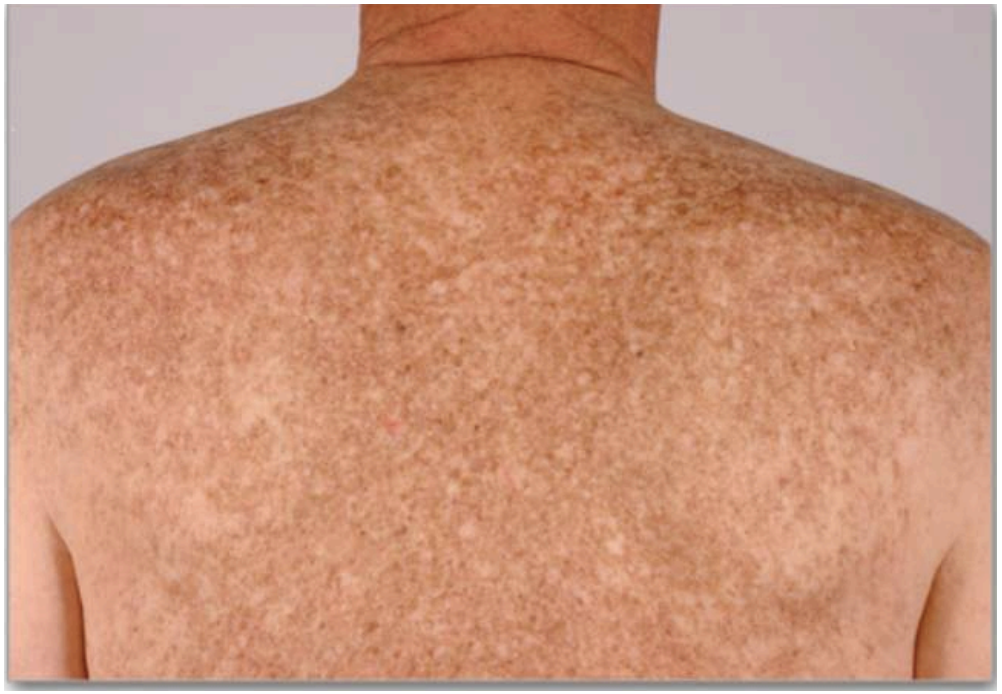
Keratosis pilaris

Pale to erythematous perifollicular papules with spiny keratotic plugs within the follicular openings

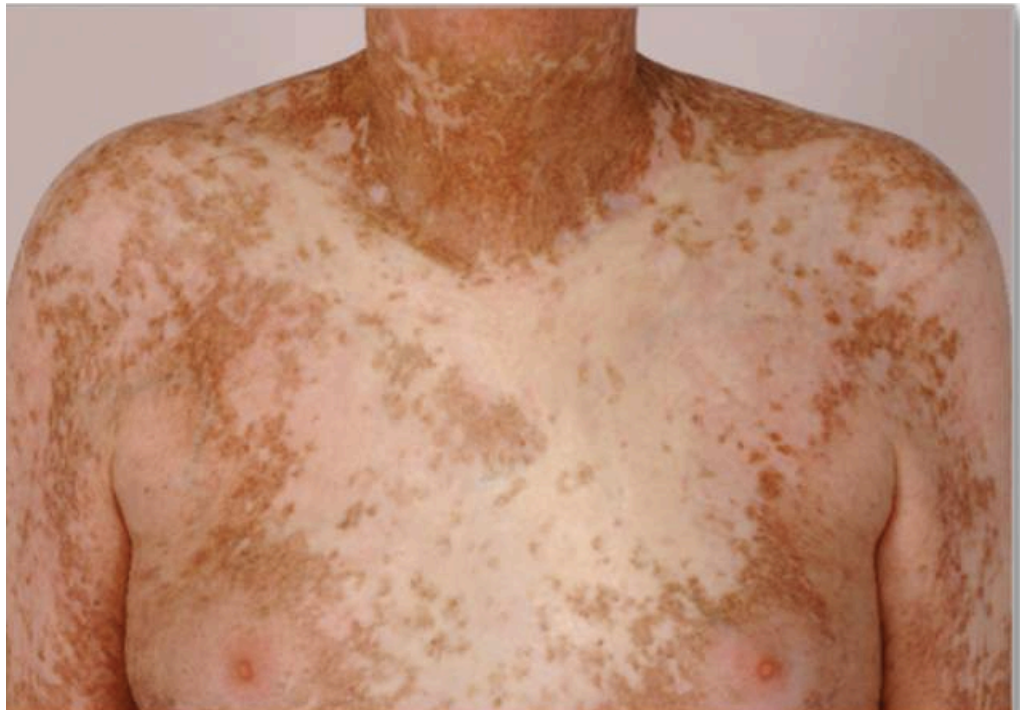


Lichen Sclerosus-like features

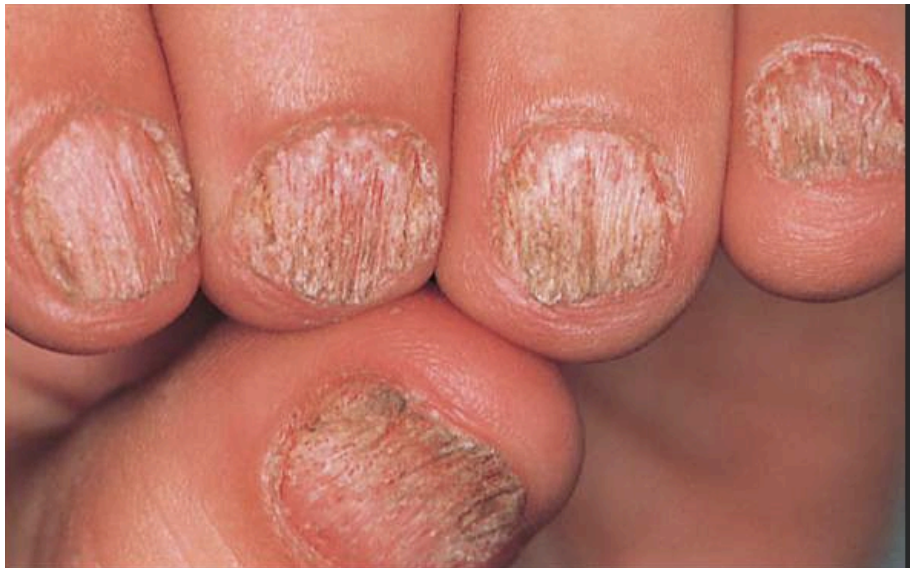
Discrete to coalescent, gray to white, moveable papules or plaques, often with follicular plugs, with a shiny apppearance and wrinkled tecture



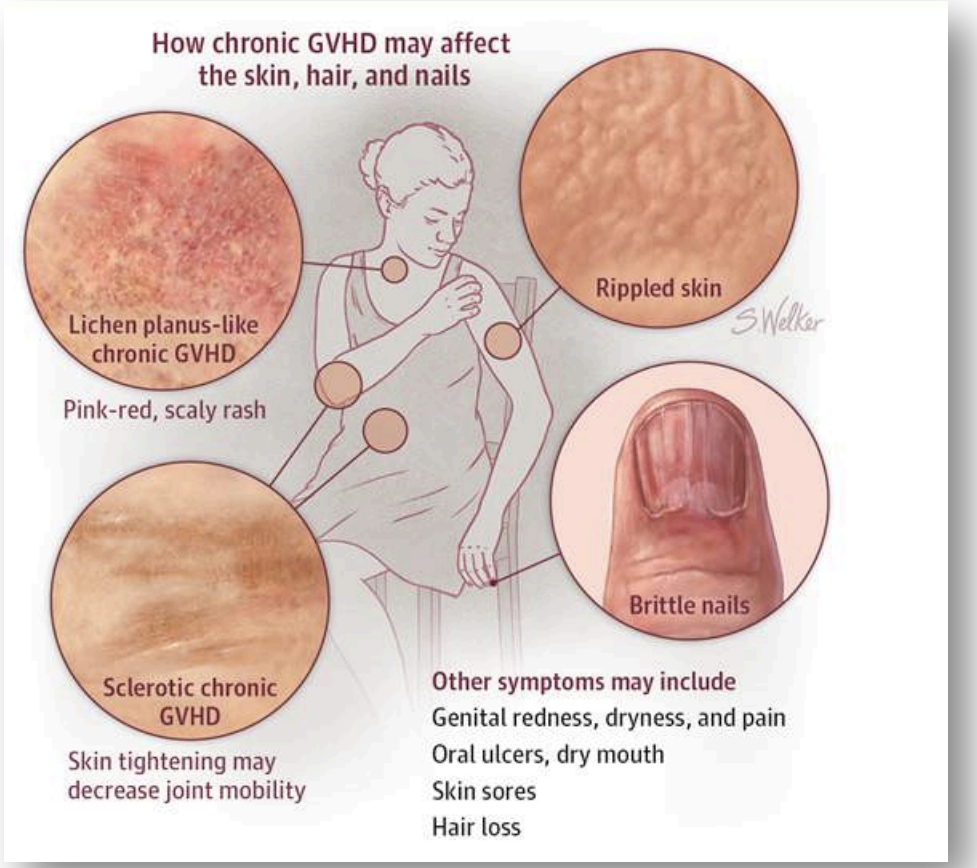
Hyperpigmentation



Hypopigmentation



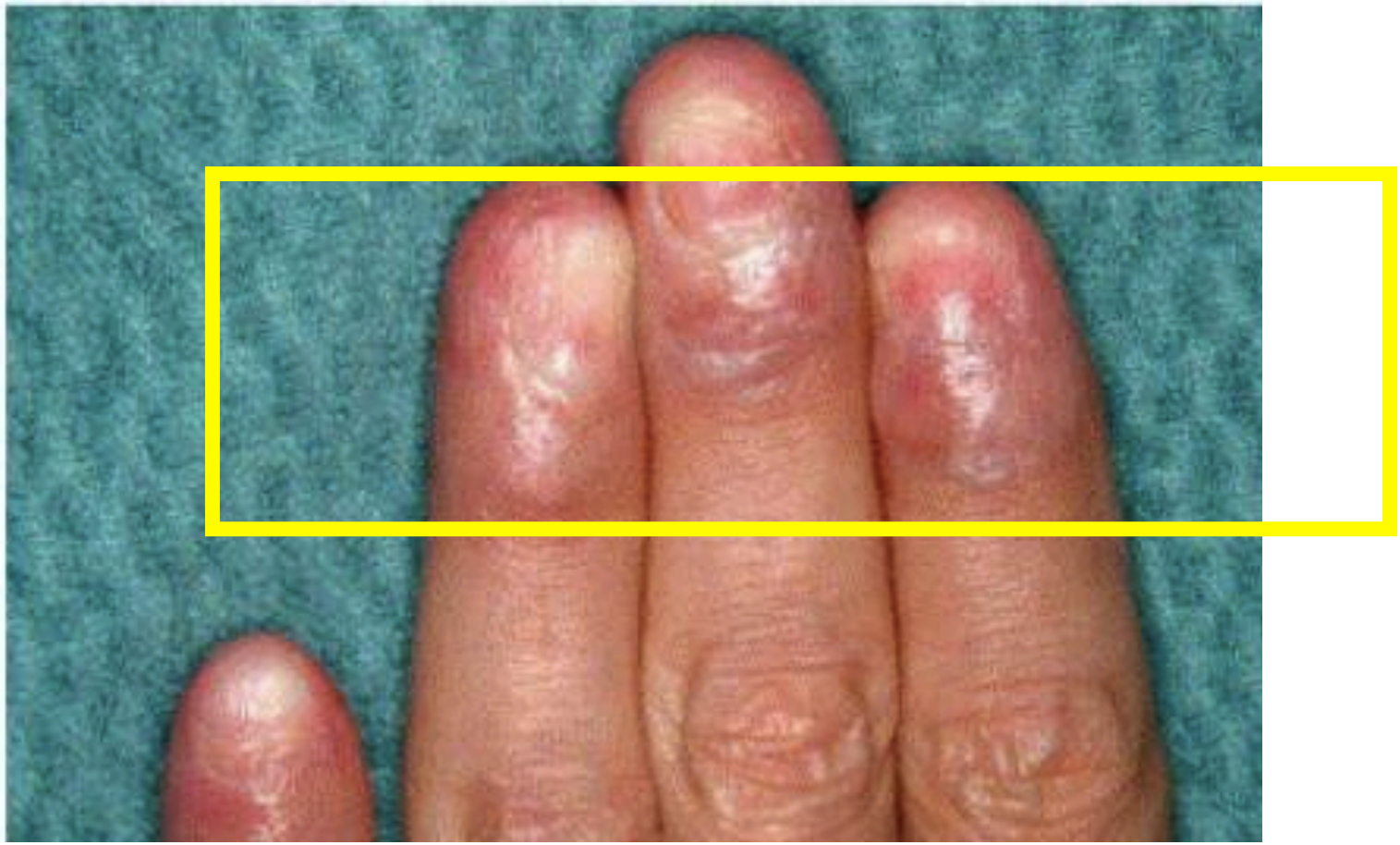
Nail Lichen-planus



Distinctive signs of nail cGVHD:

Longitudinal ridging, splitting, brittleness, onycolysis and loss of nails (usually symmetric and affecting most nails)

JAMA,2016



Periungual teleangectasia

Skin cGVHD

- Itching
- Burning
- Pain
- Atrophy
- Ulcerations
- Flakiness
- Shiny appearance
- Hyper - hypopigmentation

- Loss of sweating
- Erythema
- Vertical ridging and splitting of the nail beds
- Graying hair

Skin care aims to:

- mantain the integrity of the skin

- reduce the risk of infection

-prevent retractions and functional impairments

SKIN CARE: PRINCIPLES

- Regular application of preferred **emollients**
- If the skin is flaky, use **lipids** in addition to emollients (they nourish the skin and provide a barrier)
- If using emollients: apply steroids at least 30’ before or after to ensure effective absorbtion. If the skin is broken: do not use steroids
- Use the emollients in the right quantity (almost 500g/week in an adult pt).
- Choose the right products: ointment (lower limbs), lighter products for more delicate areas of the body (e.g. the face),.
- Use bath or shower preparation rather than soap
- Protect from the **sun**: use sunscreens

- Avoid the use of perfumes directly on the skin
- Choose the right make up (always use a moisturiser under and choose good quality products)
- Promote good personal hygiene and the importance of dry the skin before the products application. This helps the absorption of the products themselves.
- Pruritus: consider the use of systemic antisthamine
- Avoid rubbing
- Manage bleeding risk

How do i manage…?

1. RASH

emollients (higher percentage of water if pruritus is a major issue: these products can be more cooling) → regular application + patient compliance

Topical steroids

Menthol cream (in case of **pruritus.** Patient can feel cold: use only on selected areas)

Choose the right clothing: natural materials are better (cotton, silk). Loose clothes minimise the risk of friction/irritation

How do i manage…?

2. ERYTHRODERMA → widespread

Emollients and moisturing of the skin

Increase fluids intake

Skin integrity mainteinance: coconut oil or natural lipids in addition to emollients. Aloe vera is good as well (if used alone it can dry the skin)

How do i manage…?

3. BULLOUS, DESQUAMATION → loss of skin integrity

Treat as a burn: risk of infection → sterile dressings.

Pain management.

Keep the patient warm. Risk of hypothermia.

Mantain a good hydration status.

Wound care

If the skin breaks:

- Risk of infection
- Risk of bleeding
- Slower healing

Importance of shared institutional protocols for the management of GHVD lesions.

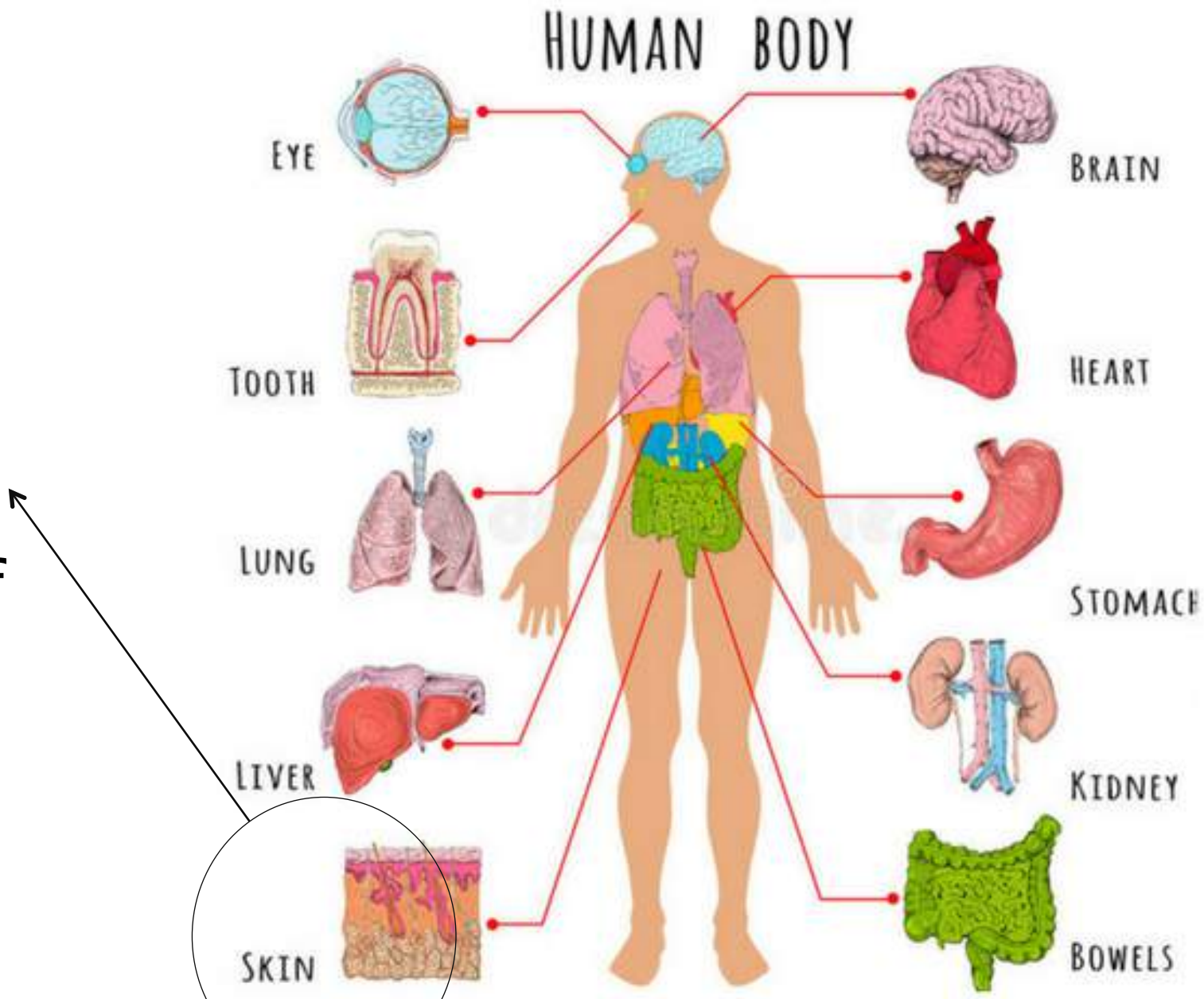
Empower the patient and involve him/her in this process of self-care.

JOINT AND FASCIA

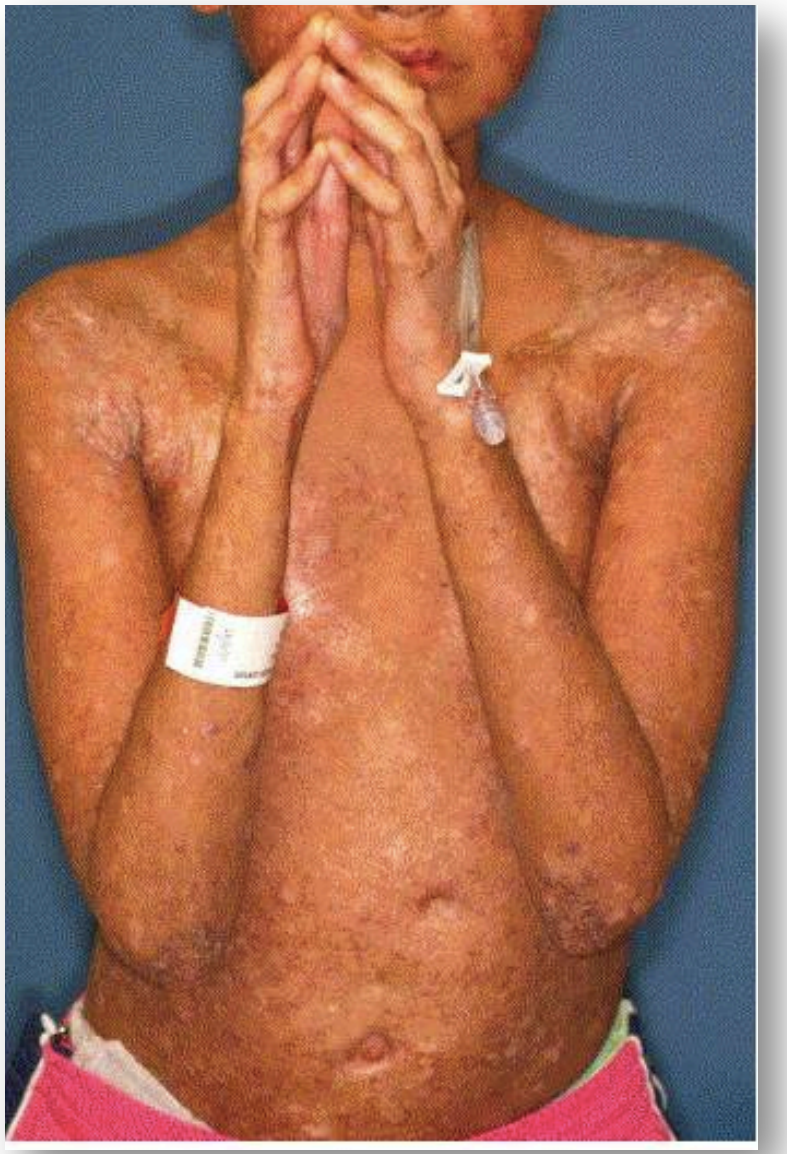
Sclerosis of ovrlying skin and subcutaneous tissue and joint stiffness or contractures.

High risk of severe impact on the Quality of Life.

What to consider:
Range of movement
Limitation of ADL



Prayer Sign



Acute limitation of wrist dorsiflexti on.

	SCORE 0	SCORE 1	SCORE 2	SCORE 3
JOINTS AND FASCIA P-ROM score *(see below)* Shoulder (1-7):___ Elbow (1-7): ____ Wrist/finger (1-7):___ Ankle (1-4):___	No symptoms	Mild tightness of arms or legs, normal or mild decreased range of motion (ROM) **AND** not affecting ADL	Tightness of arms or legs **OR** joint contractures, erythema thought due to fasciitis, moderate decrease ROM **AND** mild to moderate limitation of ADL	Contractures **WITH** significant decrease of ROM ***AND*** significant limitation of ADL (unable to tie shoes, button shirts, dress self etc.)

Abnormality present but explained entirely by non-GVHD documented cause (specify): _____

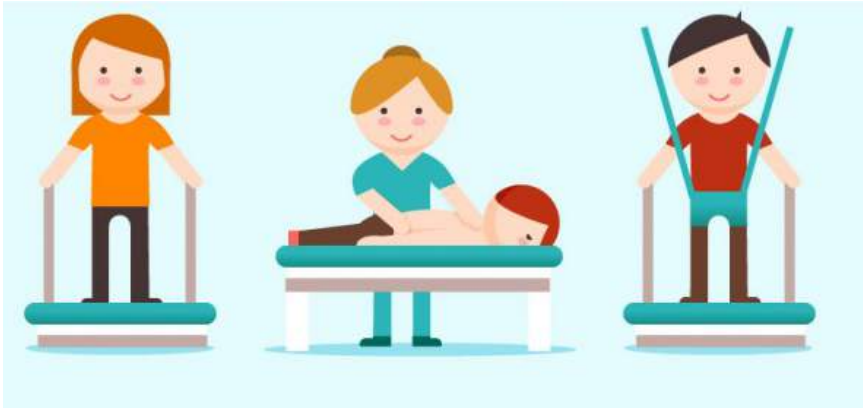
PATIENT'S FUNCTIONAL STATUS AND ORGAN IMPAIRMENT

AIM: prevenction and management of muscle loss, weakness, contractures and limb swelling.
Promotion of activities of daily living.

Regular exercises to be taught to patients and caregivers.

Regular massage to mantain flexibility and function of the affected part of the body.

Massages are useful in case of fascial involvement

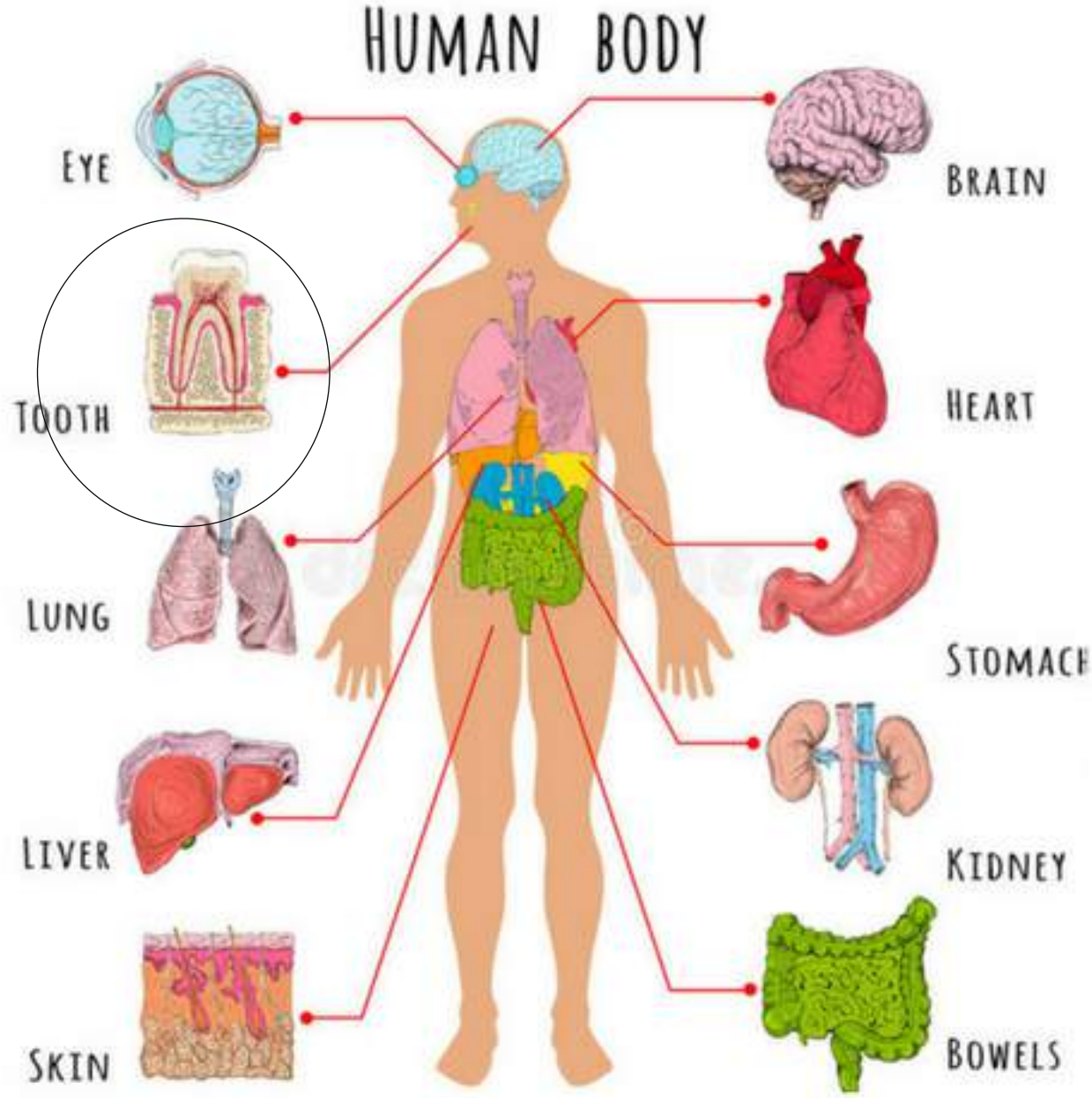


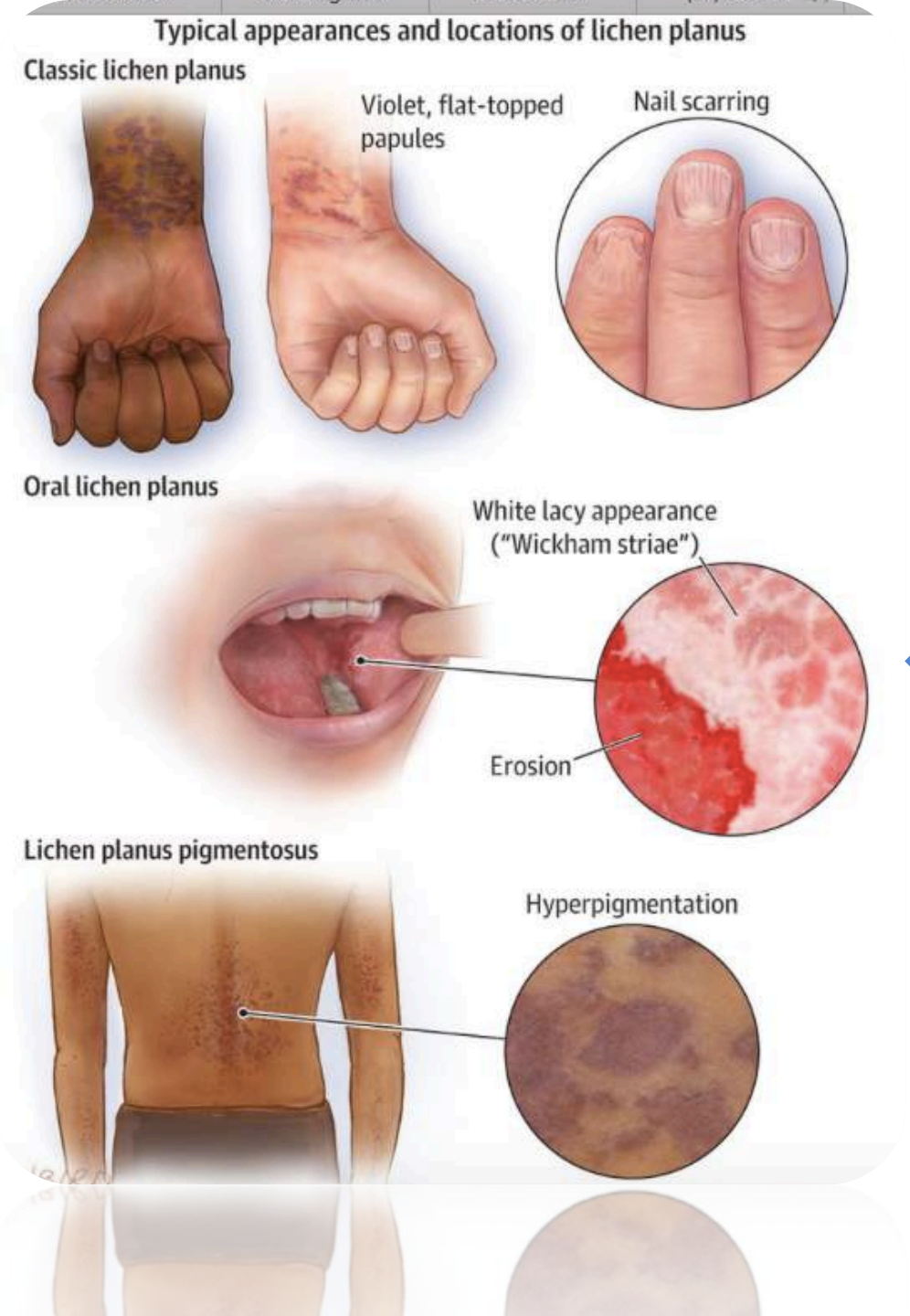
How to manage JOINT and FASCIA GVHD?

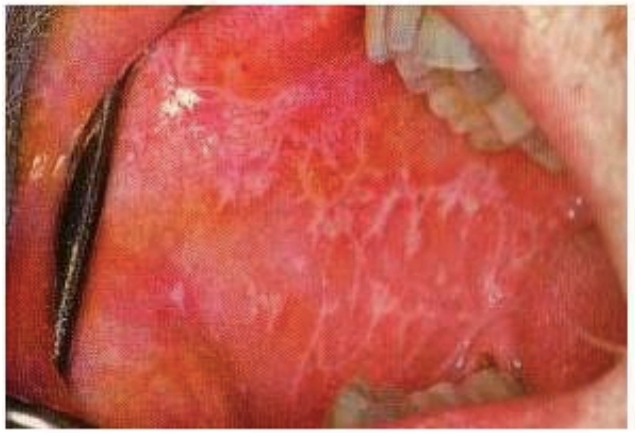
ORAL CAVITY

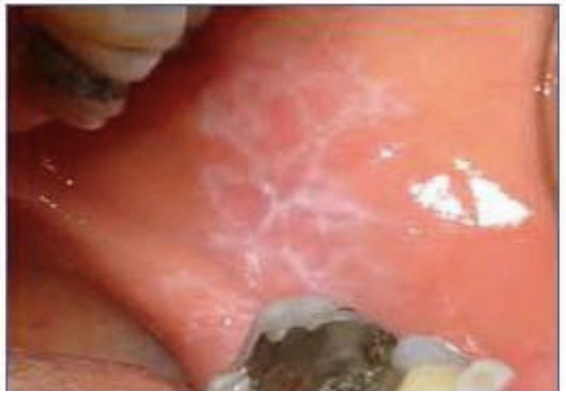
1° target in BM HSCT
2° target in PBSC HSCT

Involvement of:
a.Mucosa
b.Salivary glands
c.Mouth and surrounding tissues







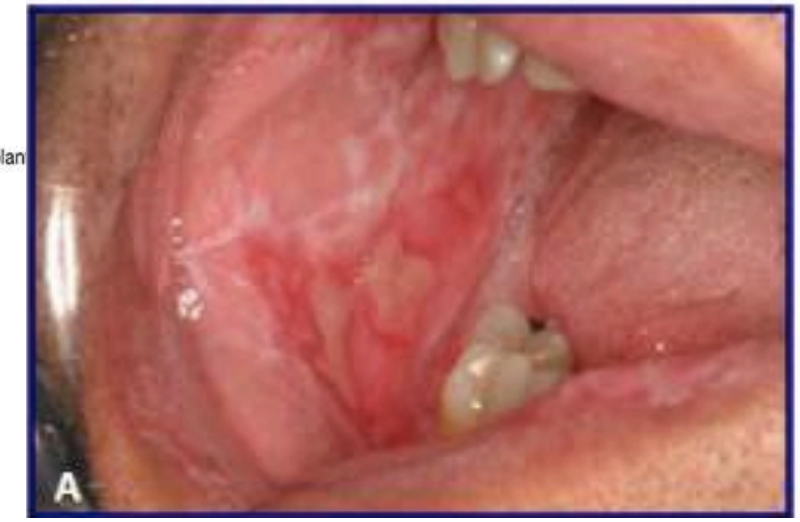


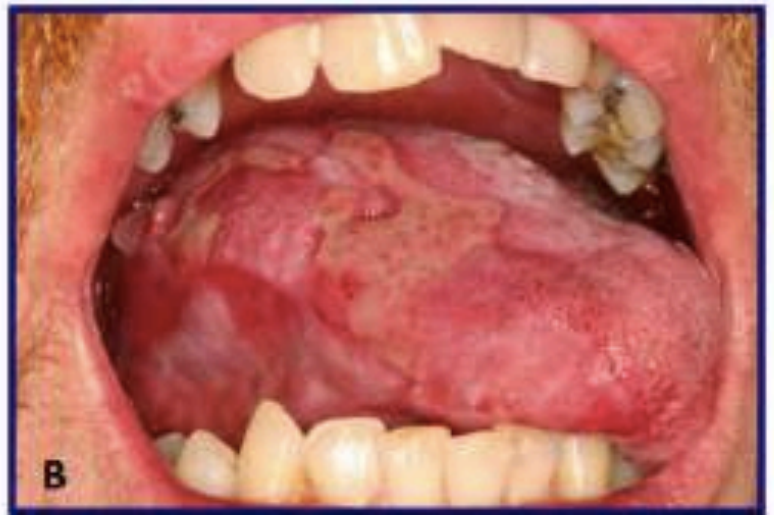
Lichen planus-like changes

White lines and lacy-appearing lesions

Or plaques

American Academy of Oral Medicine (aaom.org)





Erosive lesions

Ulcerative lesions

Dry mouth (xerostomia)

Pain

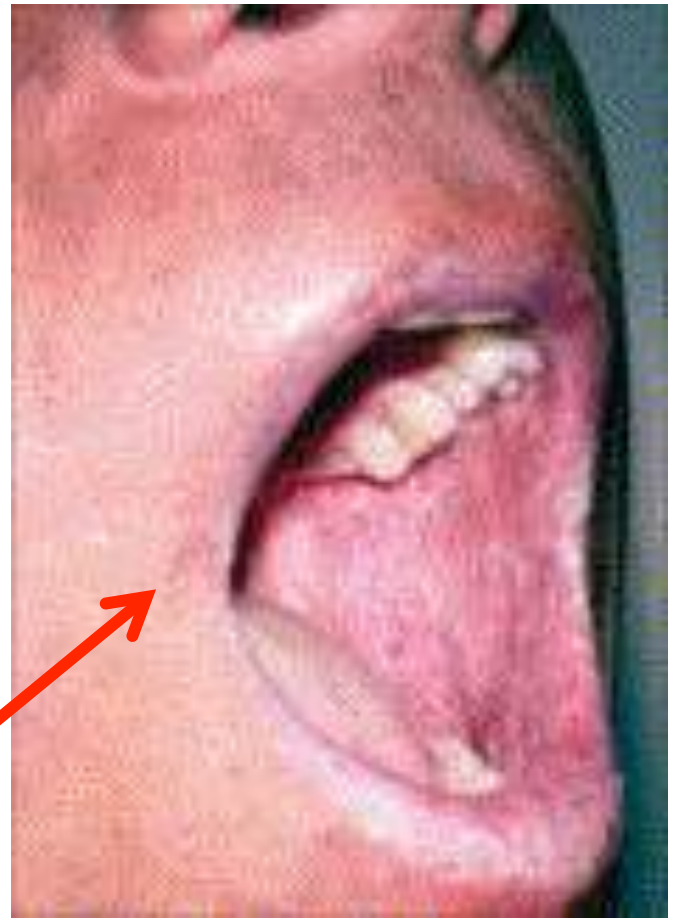
Gengivitis

Hyposalivation

Difficult chewing and swallowing food

Changes in taste

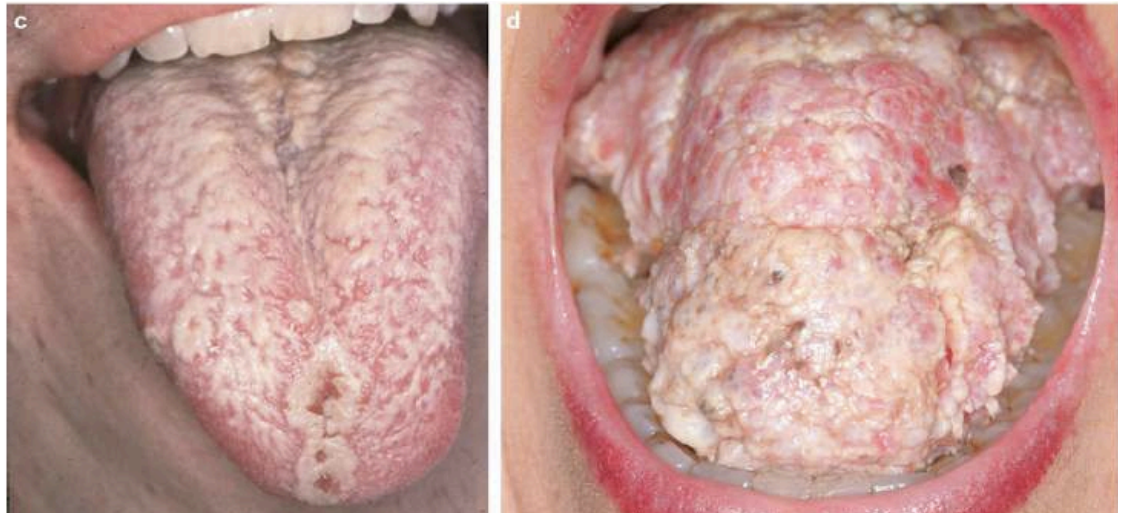
Higher risk for developing dental caries



Tightness of the skin + xerostomia

American Academy of Oral Medicine (aaom.org)

Tongue involvement



Atrophy of the tongue is related to shortened or absent lingual papillae.

Higher risk to develop a secondary malignancy (squamous cell carcinoma)

ORAL CARE PRINCIPLES

AIM: reduce symptoms severity → dryness, pain, sensitivity; mantain mucosa integrity.

Mantain a **good oral care** and hygiene: avoid products with a strong flavour that could irritate the mucosa and trigger the GVHD process.

Sip water and chew sugar-free gums to **make xerostomia better.**

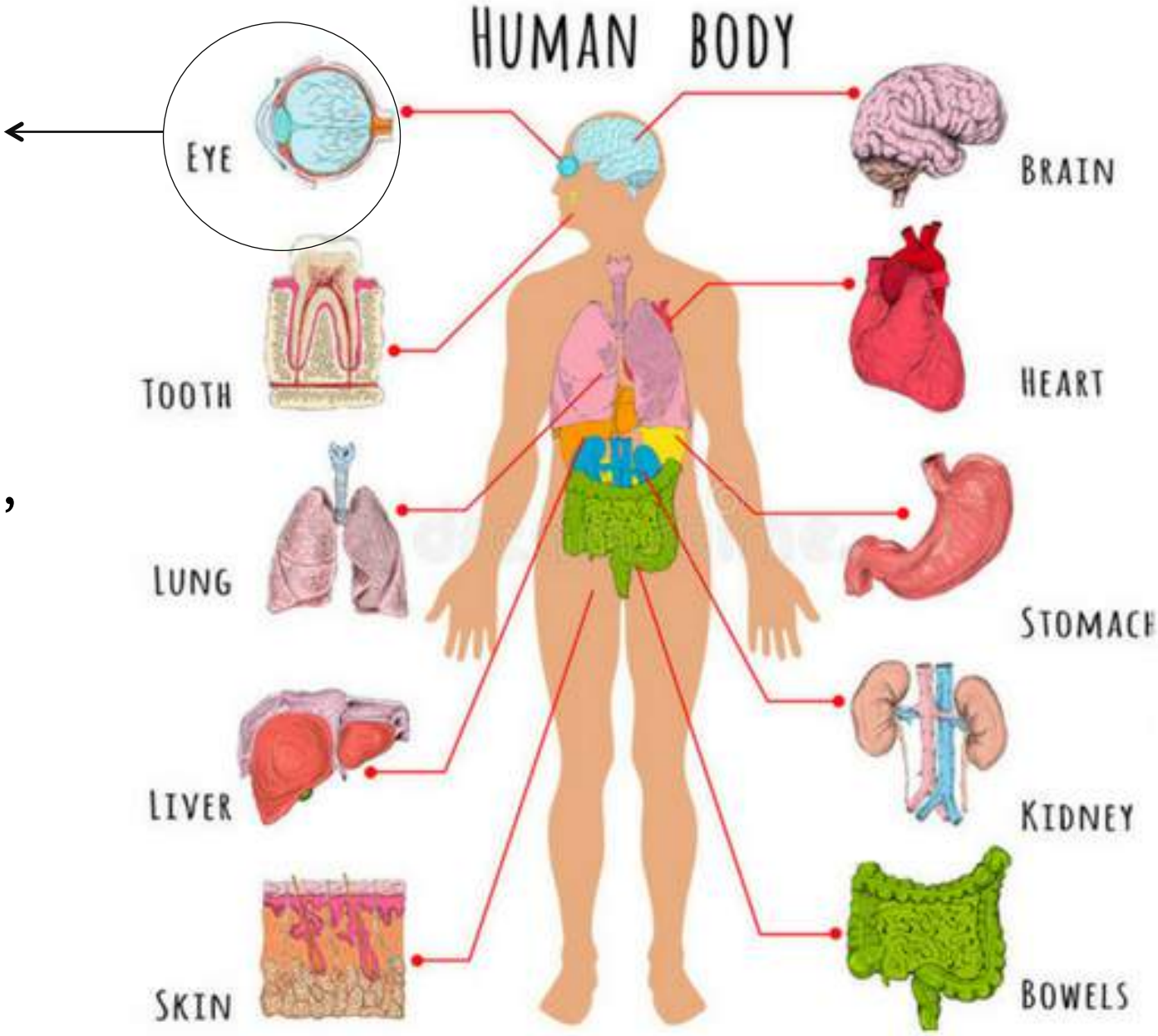
Topical steroids: mouthwashes (budesonide, MPDN, betamethasone)

Topical application of **local anaesthetics**: mouthwashes or spray (lidocaine) → check patient for compliance and awareness

EYE

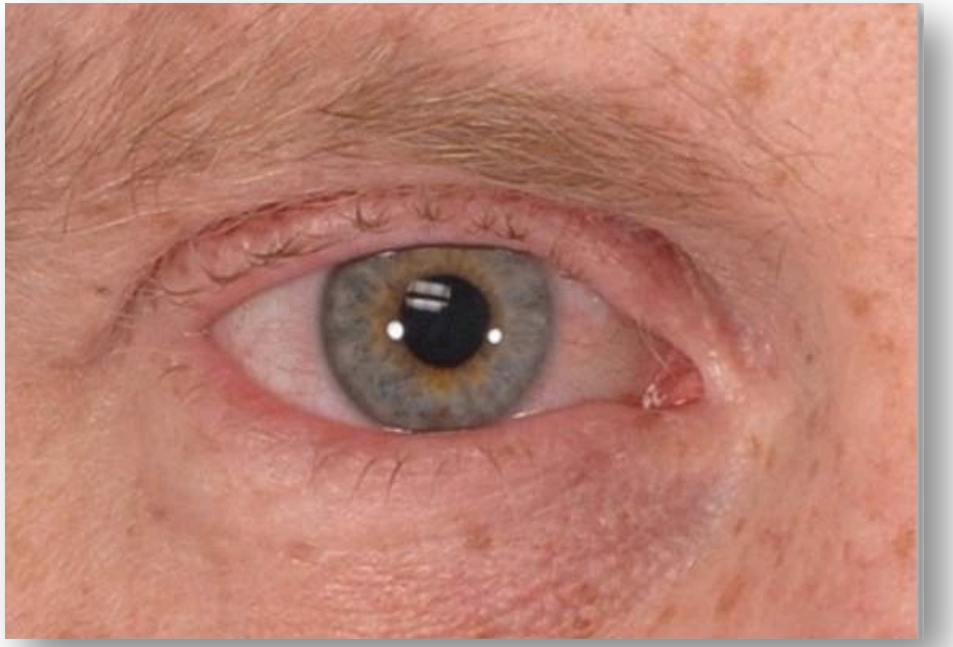
Cicatricial conjuncivitis,
keratoconjuntictivitis.
Lacrimal dysfunction.

Photophobia, burning, irritation,
pain, foreign body sensation,
blurred vision.



Local treatment for symptoms

- Lubricants, lubricants, lubricants!
- Glasses and goggles
- Therapeutic contact lens



Keratoconjunctivitis Sicca

EYE CARE

Team working: involve an optalmologist.

Avoid dry eyes**: moisturing** ocular surfaces and lubrificate it. Use preservative-free drops. Regular use of drops. **SUN protection.** Use of goggles or glasses.

Steroids drops can be useful in case of eyes symptoms flare.

CSA eye drop could be a solution but they may irritate the eye and provocate a burning sensation → reduction of **patient compliance.**

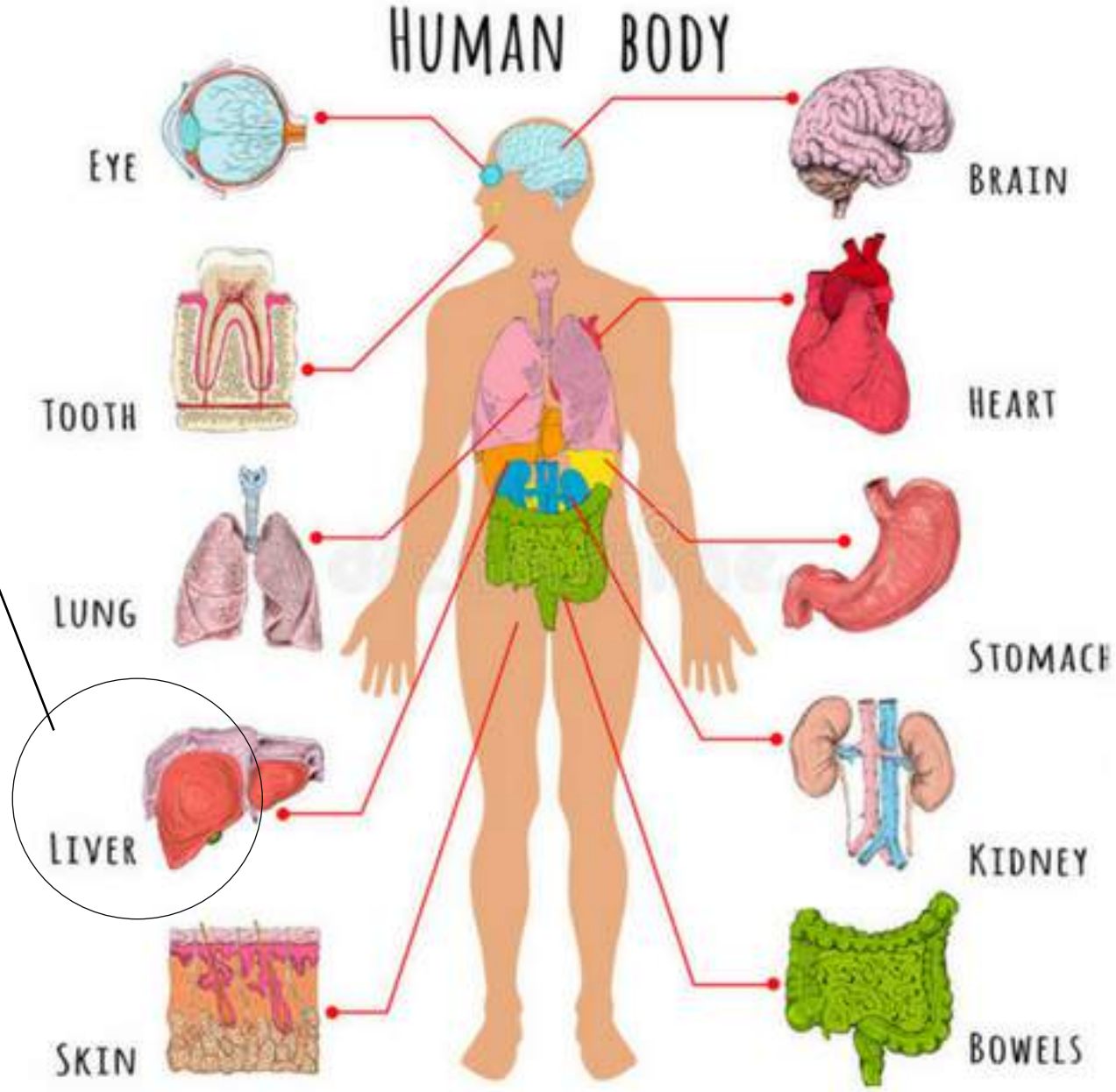
LIVER

No specific diagnostic features for chronic GVHD.

Biopsy and imaging can help clarifying the diagnosis.

Possibly present:

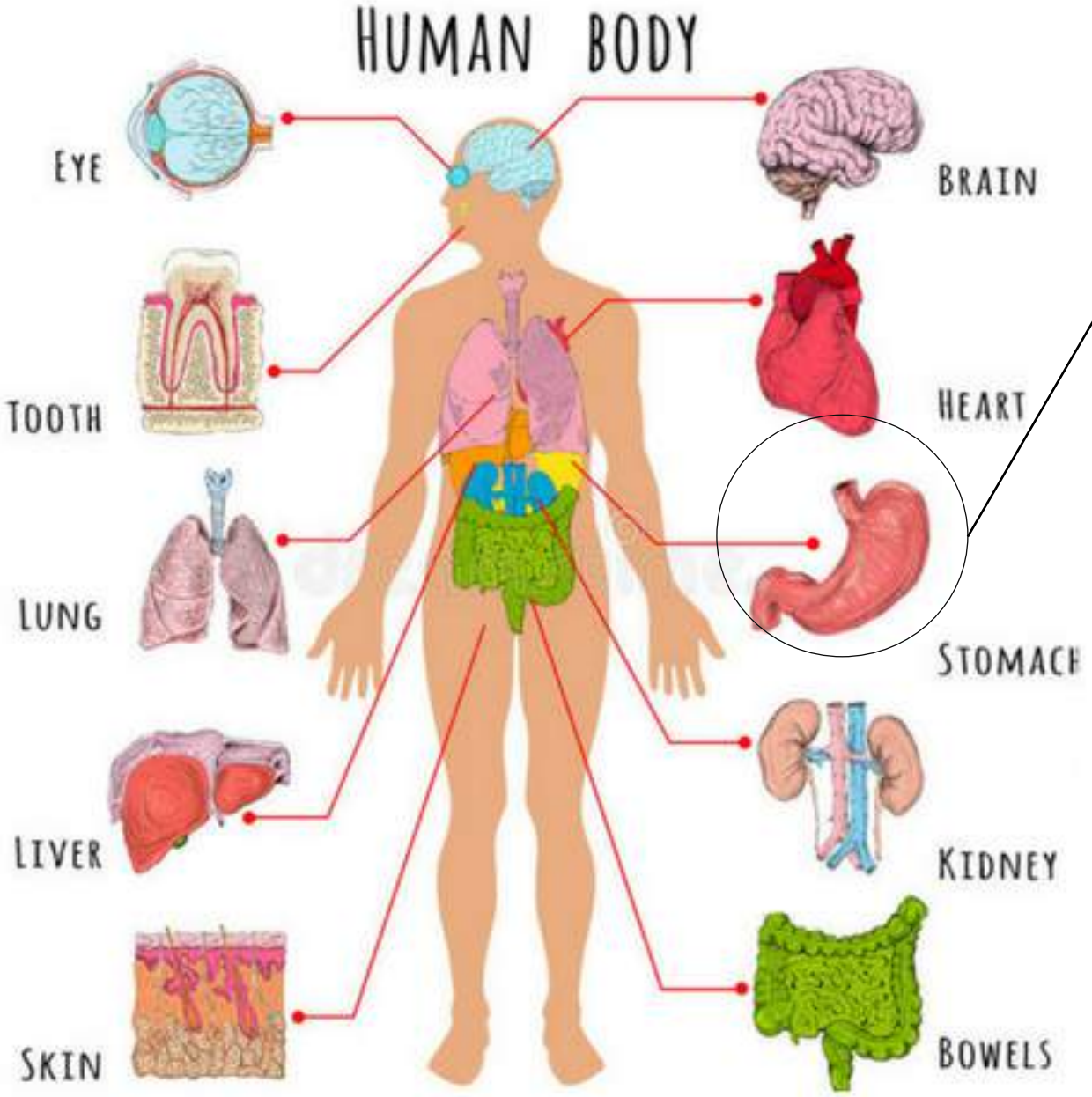
Jaundice
Malaise
Itching
Fatigue



LIVER	Normal total bilirubin and ALT or AP < 3 x ULN	Normal total bilirubin with ALT ≥3 to 5 x ULN or AP ≥ 3 x ULN	Elevated total bilirubin but ≤3 mg/dL or ALT > 5 ULN	Elevated total bilirubin > 3 mg/dL
Abnormality present but explained entirely by non-GVHD documented cause (specify):				

Possible presentations:

- rise in serum ALT with or without jaundice
- cholestatic picture (rise in serum alkaline phosfatase and GGT + jaundice)



GI TRACT

1.Esophageal Web
Smooth, circumferential ring of squamous mucosa (endoscopy or barium contrast radiograph)

2.Upper esophageal strictures or stenosis
Narrowing of the upper to mid third of the esophagus (endoscopy or barium contrast radiograph)

3.Pancreatic exocrine insufficiency
Leads to inability to properly digest food due to a lack of enzyme. It can benefit from enzyme supplementation.

Most of these symptoms are present in both acute and chronic GVHD.

- Anorexia
- Early satiety
- Nausea
- Vomiting
- Abdominal pain
- **Diarrhea** → Stools culture and virology test (Clostridium difficile? CMV?)
- Bloating
- Cramping
- Weight loss
- malnutrition
- Painful swallowing (odynophagia)
- Difficulty swallowing dry foods/pills (dysphagia)
- Heartburn

In case of GI tract involvement:

-check the stools for characteristics and quantity

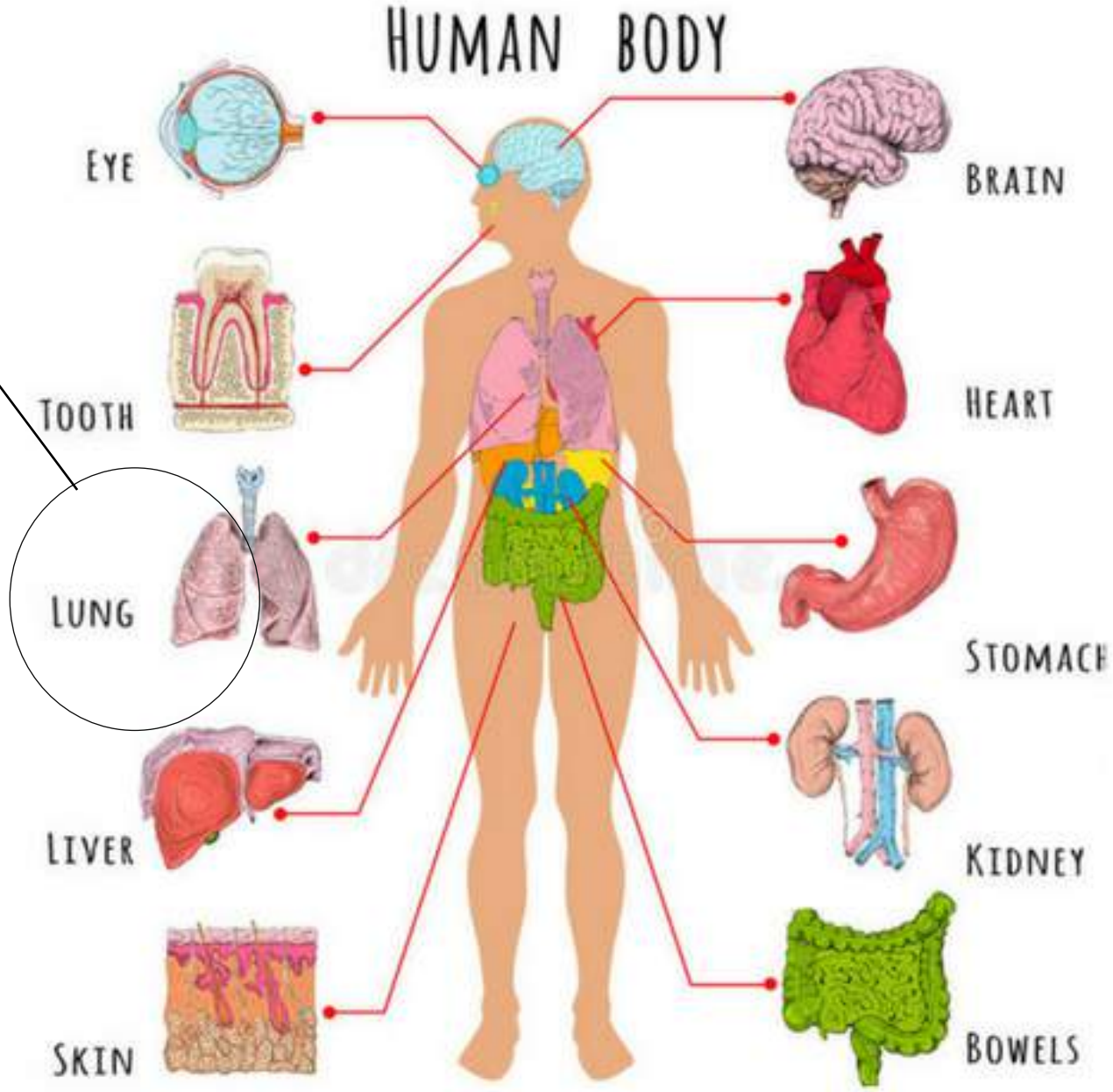
- skin care (stools can be acid and create skin lesions: barrier creams could help)
- Monitor the presence of nausea and vomiting: check the nutritional status and provide nutritional support. Oral budesonide can reduce the nausea.
- Avoid strong flavours or smells in patient room

LUNG

Bronchiolitis obliterans (BO) diagnosed with Pulmonary Function Test
Obstructive defect. Dyspnoea on exertion, cough, wheezing.

Air trapping and bronchiectasis
Air trapping on expiratory CT, small airway thickening

(distinctive sign of cGVHD but insufficient alone to diagnose it)



PATIENT-REPORTED SYMPTOMS AND SIGNS

Difficulty breathing

Wheezing

Shortness of breath at rest and/or with exertion

Dry cough

DIAGNOSTIC TEST

Pulmonary Function Test (PFT)

Expiratory CT

Pre-transplant screening is essential

PATIENT SYMPTOMS

LUNGS**				
Symptom score:	No symptoms	Mild symptoms (shortness of breath after climbing one flight of steps)	Moderate symptoms (shortness of breath after walking on flat ground)	Severe symptoms (shortness of breath at rest; requiring 0_2)
Lung score: **% FEV1** ☐	FEV1≥80%	FEV1 60-79%	FEV1 40-59%	FEV1 ≤39%

Pulmonary function tests

Not performed

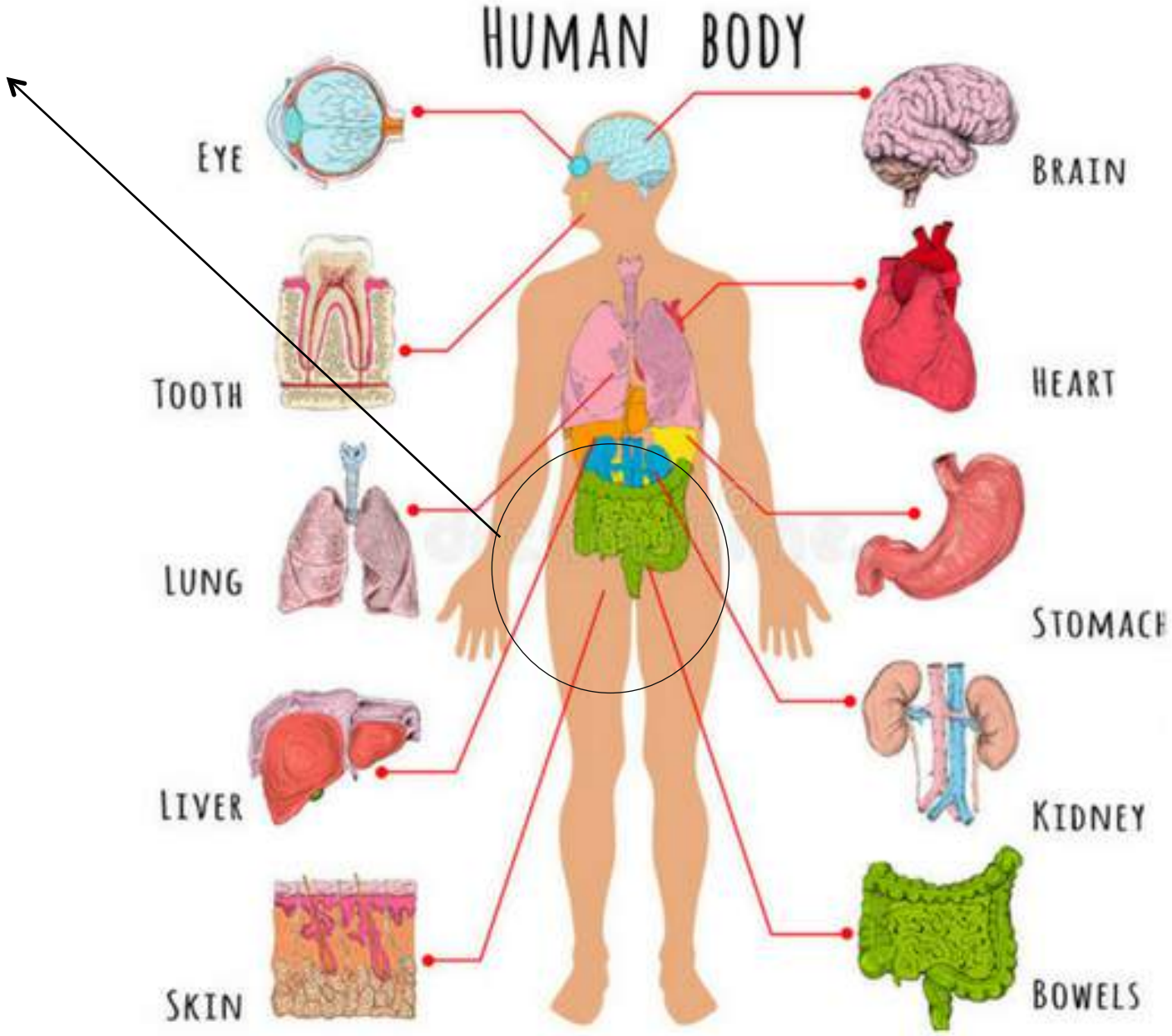
Abnormality present but explained entirely by non-GVHD documented cause (specify): _____

TEST

GENITAL TRACT

Lichen planus-like and lichen slerosis features.

Unreported symptoms by patients.

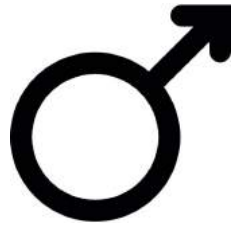


- Itching
- Painful urination (dysuria)
- Pain
- Painful sexual intercourse (dyspareunia)
- Dryness
- burning

Vaginal Scarring or clitoral/labial agglutination

A narrowing of the vagina, often with accompanying tissue changes such as dryness, loss of elasticity, adhesion ans scar tissue.

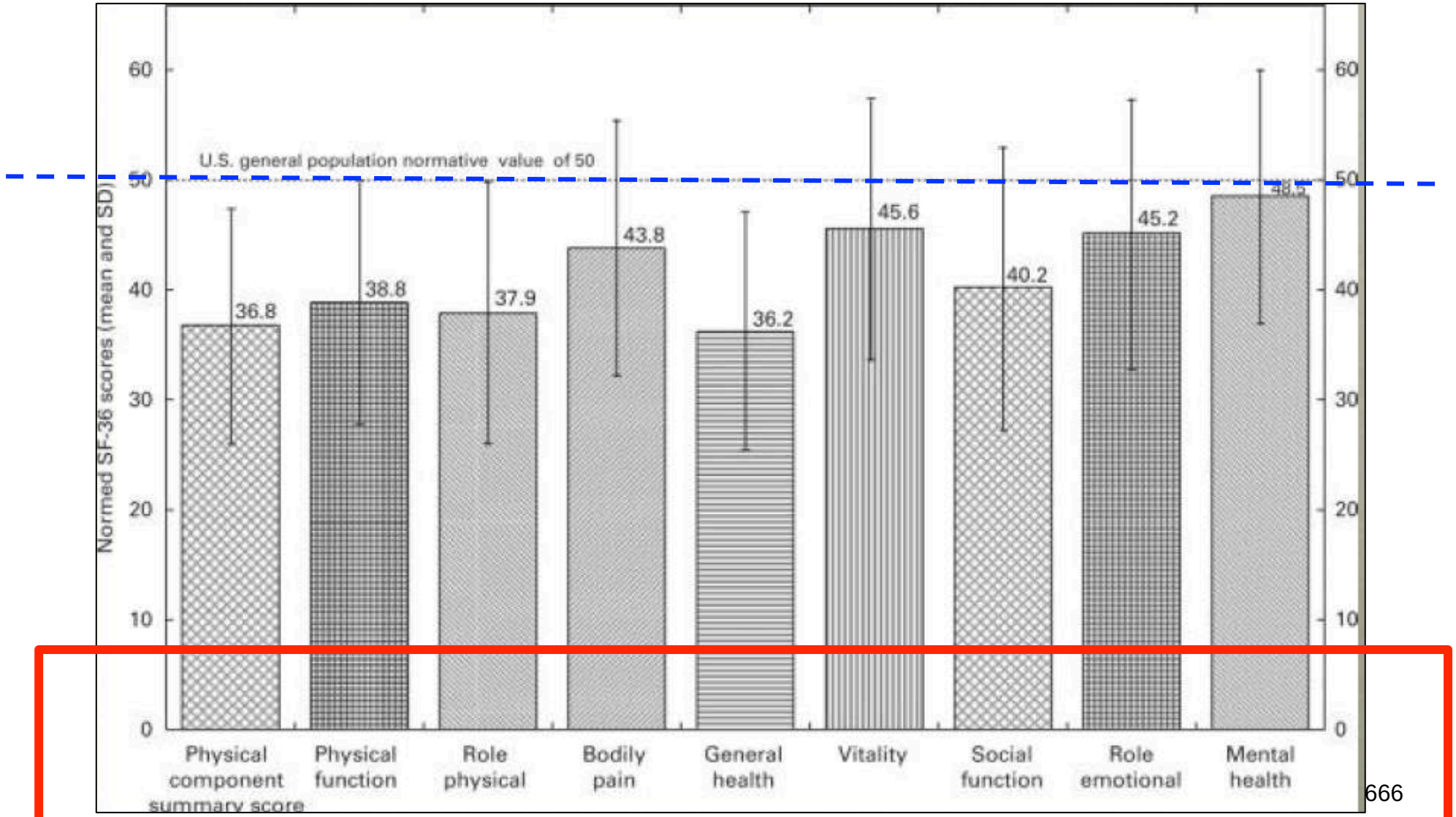
Erosive lesions and fissures of the vulvar mucosa. Patchy or generalized erythema.



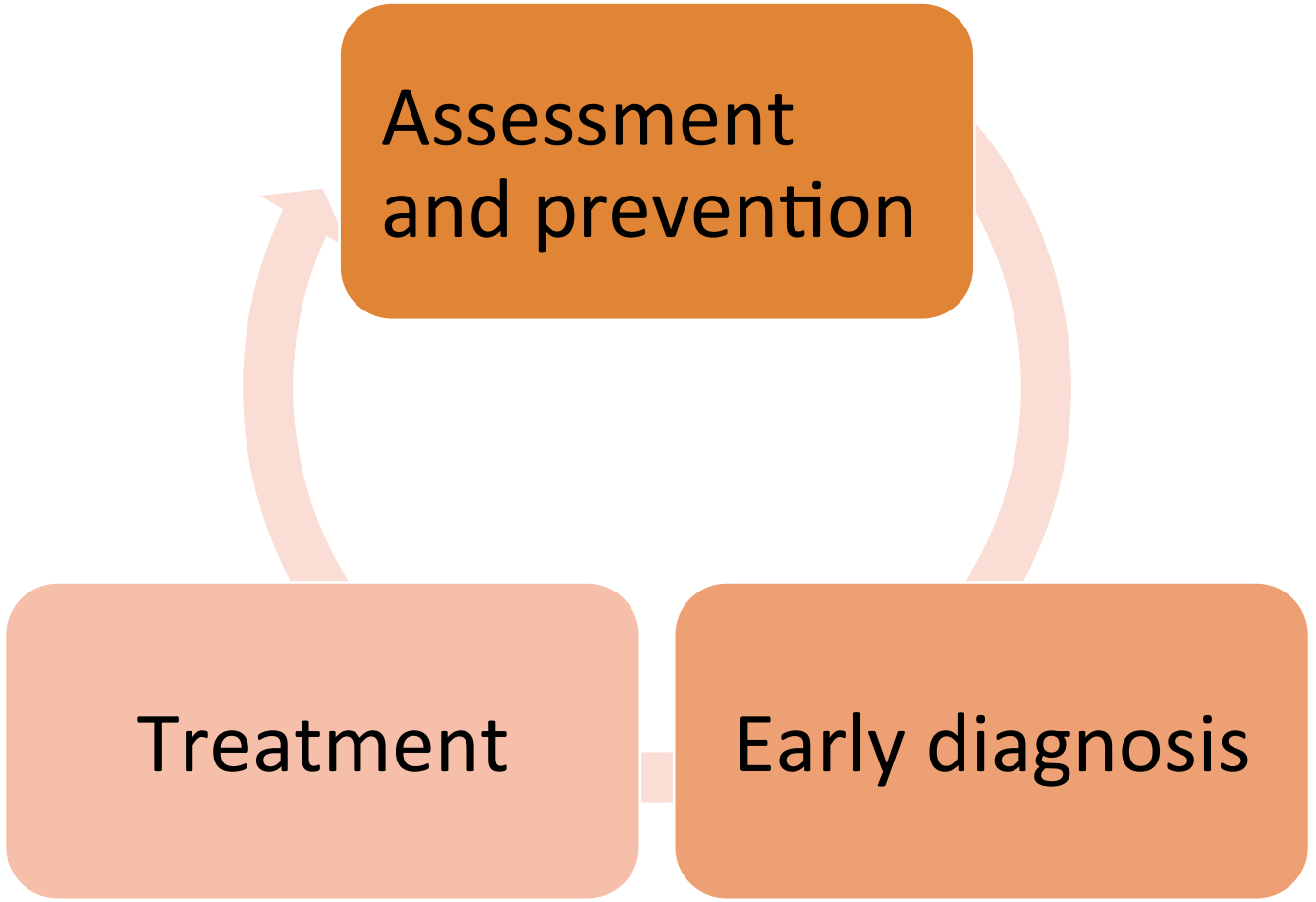
Non infectious balanoposthitis, phimosis, meatus/urethral scarring or stenosis.

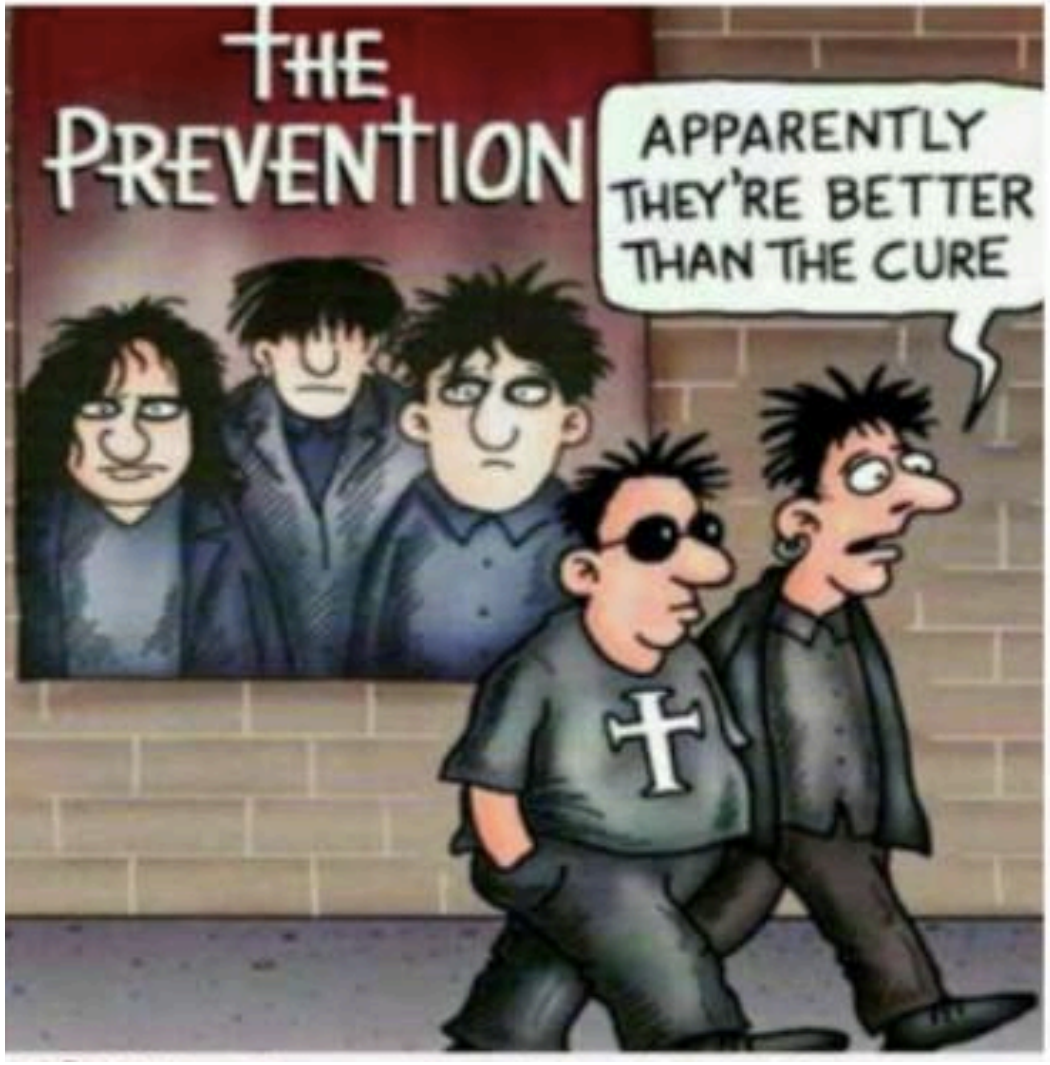
cGVHD: functional performance

(Mitchell et al, BMT 2010)



How to manage GVHD?





Prevention is always better than cure

With standard prophylaxis, almost 40% patients receiving HLA matched donors will develop GVHD requiring high dose steroids.

Ciclosporin (CsA)

Immunosuppressor.

It reduces the activity of the immune system by interfering with the activity and growth of T cells. It does not affect B cell function and the production of antibodies.

Given 1-2 days before the HSC infusion, as an intravenous administration. Then, it turns to oral (both capsule or syrup→ children).

SIDE EFFECTS: hypomagnesemia, hypertension, hirsutism, headache, nausea and vomiting, skin rash, nephrotoxicity.

Need to check drug dosage in the blood. Use a dedicated line. Be aware of the risk related to the blood withdrawal from the line of CSA infusion.

Mycophenolate mofetil (MMF)

Immunosuppressor.

It selectively inhibite the synthesis and proliferation of lymphocytes.

It causes less mucosites and faster neutrophil recover compared to MTX.

Usually administered in Reduced Intensity Transplant Conditioning regimen (RIC).

Methotrexate (MTX)

Antiproliferative agent.

It prevents the division and the proliferation of T cells.

Given, IV, on day: +1, +3, +6 and +11.

In case of severe mucositis, the IV dose is not administered.

! PPI for staff preparing and administering the cytotoxic drug.

ATG

It decreases T cells.

It can lead to viral infections (especially reactivation of EBV!)

SIDE EFFECTS: allergic reactions during infusion, fever, rash. Blood test: rise of procalcitonine

Conclusion

- Early recognition
- Nursing care challenges
- Continuity of care
- Shared protocols
- Team working – Shared competences
- Caregivers and patients involvement: partnership
- Supportive care
- Promote the quality of life

Literature reference

- Sousa IC et al (2013) Skin signs of GVHD (J Bone Marrow Res, 1:134)
- Corien EW (2016) Graft-vs-Host Disease (JAMA 152 (3): 356)
- GVHD: a learning module for nurses (2018, www.oncolink.org)
- Jagasia MH et al (2015) NIH consensus development project on criteria for clinical trials in cGHVD: The 2014 diagnosis and staging working group report (Biol Blood Marrow Transplant, 21 (3): 389-401)
- Villarreal CD et al (2016) Cutaneous graft-versus-host disease after HSCT- a review (An Bras Dermatol. 91(3): 336-43)
- Hymes et al (2006) Cutaneous manifestations of chronic GVHD (Biol Bl Marrow Transpl 12: 1101-1113)
- Kenyon M, Babic A (2017) The European Blood and Marrow Transplantation Textbook for nurses, Springer Open

EBMT European Society for Blood and Marrow Transplantation

Evaluation of post-transplant cellular therapy outcomes

Michelle Kenyon
Consultant Nurse (BMT)

EBMT Training course
Mumbai, India
14th and 15th December 2018

Learning outcomes

Diagnosis and management of HPC graft failure

Evaluation of late effects of allogeneic and autologous transplantation

Survivorship & quality of life

Diagnosis and management of HPC graft failure

STANDARD:

B3.3.4.26 Diagnosis and management of HPC graft failure.

B3.3.4.28 Evaluation of post-transplant cellular therapy outcomes.

Evidence:

It is recognized that outcomes may not be completely understood for investigational cellular therapy studies. In these cases, investigative approaches and endpoints must be defined by the investigator.

Graft failure (GF)

- major complication associated with a dismal prognosis
- incidence relatively low
- hgher risk in recipients of alternative donor HSCT

Ayas et al. 2015

- important contributor to morbidity and mortality after allogeneic SCT
- patients experiencing GF have a lower probability of survival in comparison to those with sustained engraftment of donor cells

(Olsson et al. 2013; Locatelli et al. 2014

definition

the lack of hematopoietic cell engraftment following autologous or allogeneic SCT

Lowsky and Messner 2016

classically divided into primary or secondary graft failure

primary graft failure

- defined as no evidence of engraftment or haematological recovery of donor cells, within the first month after transplant, without evidence of disease relapse

secondary graft failure

- refers to the loss of a previously functioning graft, resulting in cytopenia involving at least two blood cell lineages

Primary graft failure is usually associated with a more significant risk of morbidity and mortality in comparison with secondary graft failure

Olsson et al. 2013; Kato et al. 2013

Graft rejection

immune-mediated rejection of the donor cells by residual host cells because of genetic disparity between the recipient and the donor.

Immunological rejection of the hematopoietic stem cell graft is a major cause of graft failure

Olsson et al. 2013

graft rejection is usually defined by the absence of donor cells in a patient with pancytopenia and reduced marrow cellularity

diagnosis

- Routine monitoring of donor cell engraftment is recommended
- evaluation of chimerism status crucial for early diagnosis and optimizing the chance of rescuing patients from GF

- should be carried out routinely especially in patients who have inadequate marrow function and might be candidates for donor lymphocyte infusion (DLI) or a second transplant

(Martin 2016)

risk factors for GF

HLA disparity

ABO-mismatching in the donor/recipient pair

reduced-intensity conditioning

primary diagnosis

graft source

cell dose

graft manipulation

Treatment options

- changes to immune suppression
- DLI
- CD34+ boost
- growth factors
- second transplant

Nursing care

- physical care
- emotional support for the patient and family
- accurate, timely information about procedures, symptoms, and feelings that the transplant recipient may experience or is experiencing
- support and education on the diagnosis of GF, treatment options, and decisions regarding the care plan
- all information must be individually tailored to the patient and family needs

(Wilson and Sylvanus 2005).

- possibility of GF should be discussed prior to transplant
- patient should be counselled with regard to the risk factors for developing GF

Evaluation of late effects

“

STANDARD:

B3.3.4.29 Evaluation of late effects of cellular therapy.

”

EBMT European Society for Blood and Marrow Transplantation

Late Effect:

‘A health problem that occurs months or years after a disease is diagnosed or after treatment has been administered. Late effects may be caused by the primary disease or its treatment, and may include physical, mental, or social problems and/or secondary cancers’.

59-year old male
26 years after allogeneic HSCT

Chronic myeloid leukemia in chronic phase – Allogeneic HSCT at 37-years of age

conditioning with TBI, cyclophosphamide and etoposide

persisting complete molecular remission since 1991

Long-term follow-up

2 years - cataract, surgical repair

3 years - infertility and gonadal insufficiency (remarried)

6 years - osteopenia (osteodensitometry)

Over the years, cardiovascular risk factors

Overweight (BMI 27 kg/m2)

Dyslipidemia, arterial hypertension

No physical activity

18 and 20 years, basal cell carcinoma, complete excision

24 years, myocardial infarction

59-year old male
26 years after allogeneic HSCT

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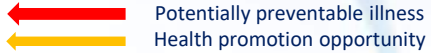


STANDARD:

B7.12 There shall be an infrastructure and policies or Standard Operating Procedures in place for provision of appropriate long-term follow-up, treatment, and plans of care.

B7.12.1 There shall be policies and Standard Operating Procedures for monitoring by appropriate specialists of recipients for post-cellular therapy late effects, including at a minimum:

B7.12.1.1 Endocrine and reproductive function and osteoporosis.

B7.12.1.2 Cardiovascular risk factors

B7.12.1.3 Respiratory function

B7.12.1.4 Chronic renal impairment

B7.12.1.5 Secondary malignancies

B7.12.1.6 Growth and development of pediatric patients

Long-term follow-up is essential for detecting and managing late effects of cellular therapy and it requires expertise that is different from that for acute care of recipients.

.

Late effects models

A dedicated survivorship clinic for cellular therapy survivors is highly recommended

The Clinical Program shall have the responsibility to either perform long-term follow-up by themselves or monitor long-term follow-up data of its former recipients already discharged to the referring physicians

In the latter case, it will still be the responsibility of the program to coordinate the long-term care with the referring physicians so that the recipients will not be lost for follow-up

Implementation challenges of LTFU care: *'Mind & Body'* approach

late-effects surveillance/ prevention

Second malignancy screening

Treatment consequences

eg organ damage, endocrine dysfunction, infection/immunisation, sexual issues, psychosocial problems

Health promotion opportunities

eg weight management, smoking cessation, exercise

recovery package

Holistic Needs Assessment (HNA)

Care Planning

Treatment Summary

Health & Wellbeing Intervention

Late effects may include:

endocrine

- new onset diabetes
- thyroid dysfunction
- hypogonadism

secondary cancers

reproductive function

osteoporosis

chronic renal impairment

cardiovascular risk factors

- hypertension
- dyslipidemia
- metabolic syndrome
- lifestyle factors

respiratory function

Screening (Majhail 2012)

Disease assessment	• MRD, chimerism
Infections	• recent history • prophylaxis
Immunisation	• revaccinations • annual flu jab
Cardiovascular	• Lipid profile, Diabetic screen, smoking history, girth measurement, blood pressure
Respiratory	• General enquiry • Lung function (FV loops, TlCO)
Endocrine	• Thyroid • Sex hormones
Bone health	• DEXA scan

Skin/ mucosa	• ongoing/ new concerns
Renal/ urinary	• symptom enquiry, nocturia, dysuria
Liver	• Ferritin, chelation
GI	• Bowel health
Ophthalmology	• cataracts
Oral health	• Dentition, oral screen
Medication	• Adherence
Second malignancy screening	• Breast, cervical, skin, bowel
Health promotion	• Weight, exercise, employment, relationships, sexual function, smoking, alcohol

Referral pathways

effective screening underpinned by multidisciplinary referral pathways

- grows specialist expertise
- expedites referral process
- ‘extension’ of HSCT team
- reduces patient anxiety
- facilitates development of pathways for physical and psychological care

Survivorship

Living with, living beyond, living well)

background

- cancer as a long term condition
  - how cancer can learn from other LTCs....and how other LTCs can learn from cancer
- living with, living beyond, living well
  - the challenges of life after cancer treatment
- person-centred care
  - using clinical assessment tools & patient reported concerns to plan care collaboratively

Cancer as a long-term condition

how cancer can learn from other LTCs…..
….and how LTCs can learn from cancer

long term conditions

Approximately one in four

of those who have been diagnosed with cancer face poor health or disability after treatment

many of these problems persist for at least 10 years after treatment and can be significantly worse than those experienced by people without cancer **

One in four people – that's 15 million (UK)

living with a long term condition

spending a large amount of their time managing their care and support

people with long term conditions including those who have had cancer experience both physical and mental effects

***Macmillan Cancer Support (2013) Throwing light on the consequences of cancer and its treatment*

case for change

People with LTCs are intensive users of health and social care services, including community services, urgent and emergency care and acute services

Common LTC's

coronary heart disease
heart failure
stroke
hypertension
diabetes
COPD
epilepsy
Cancer
mental health conditions
asthma

(DoH 2008)

cancer as a LTC….

Specific issues for patients with cancer that would benefit from a holistic, LTC approach

15 months after diagnosis people with cancer had:

- 60% more A&E attendances
- 97% more emergency admissions
- 50% more primary care contacts vs population of the same age/gender
- 64% of people living with cancer have practical or personal support needs
- 78% have emotional support needs *(Nuffield Trust 2014)*

the majority (75%) say these needs caused by their cancer or treatment

(Five Year Forward View, DoH 2016)

Living with, living beyond, living well

the challenges of life after cancer treatment

Unmet needs of survivors

one in three cancer survivors experience moderate to severe unmet needs at the end of treatment

for **60%** of people, needs not improved six months after treatment [1]

people with cancer experience **persistent long-term problems**

even those with no other long-term conditions have **poorer quality of life** scores when compared to the general population [2]

1.Armes J, Crowe M et al. Patients' Supportive care needs beyond the end of cancer treatment: A perspective, Longitudinal survey. Journal of Clinical Oncology. 2009.27(36):6172–6179. 3 Glaser A, Fraser L et al. (2013)

2.Patient Reported Outcomes of cancer survivors in England 1-5 years after diagnosis: a cross sectional survey. BMJ Open. 2013. e002317. Published online April 12 doi: 10.1136/ bmjopen-2021-002317

lost in transition

£5.3 billion lost to business pa

92% lose income

40% QoL impact

33% future and health worries

20% psychosocial difficulties

Cancer – the main concerns

Clinical concerns

- chronic fatigue
- sexual difficulties
- mental health problems
- pain
- urinary and gastrointestinal problems
- lymphoedema

Holistic concerns

1. Worry, fear or anxiety
2. Tiredness / exhaustion or fatigue
3. Sleep problems / nightmares
4. Pain
5. Eating or appetite
6. Anger or frustration
7. Getting around (walking)
8. Memory or concentration
9. Hot flushes / sweating
10. Sore or dry mouth

(HNA data - Macmillan 2015)

Concerns are important for well-being

more concerns people (with cancer) have the more distressed they feel

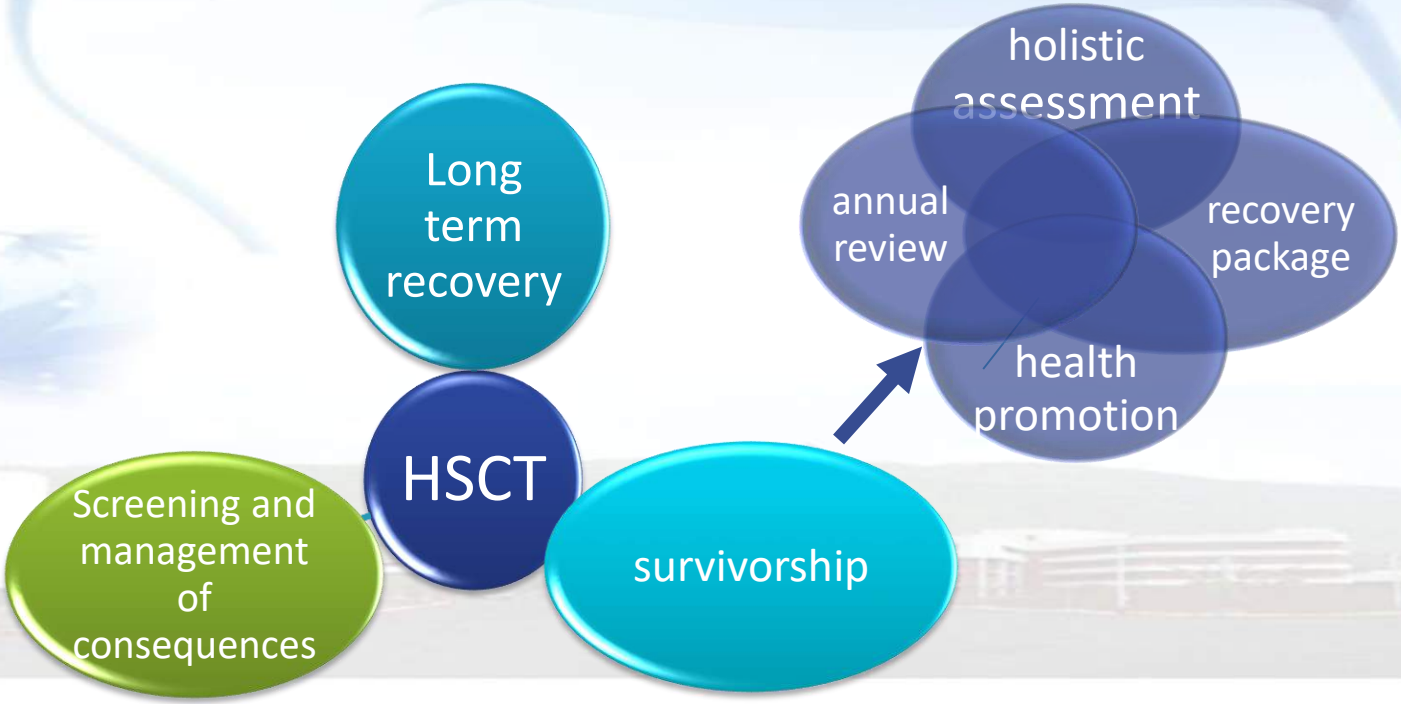
it can be difficult for people to discuss what's worrying them….

.....or for healthcare professionals to pick these concerns up

Person-centred care

using clinical assessment tools & patient reported concerns to plan care collaboratively

Late complications and beyond



Range of issues

Not all complications are physical

cancer and work

Patients benefit from **early** support considering work and education options *(NCSI 2013)*

Return to work is associated with

- higher self-reported general health
- improved well-being
- good quality of life

Work is extremely important to survivors and has health benefits

Baker 1999, Andrykowski 2005, Gielissen 2007, Bieri 2008, Snyder 2002, NCSI 2013

54% of patients in paid work 1-3 years post transplant vs 69% for all cancers combined *(Anthony Nolan 2015)*

working individuals

good performance status

report low distress levels

few concerns

Proportion working survivors declines with age notably from age 44

Appropriate group to target return to work interventions

Interventions addressing return to work issues benefit individuals and society

- Volunteer work, CV development
- Phased return (fatigue, concentration)
- Flexible working/ home based office days

Employed individuals less costly for the state and consume less health and social care than non-working counterparts

range of interventions

Nursing considerations – longer term and beyond

late recovery

- complex for some
- complications can persist
- Acute/ chronic illness (infection, GvHD)
- ongoing vigilance critical to outcome

nursing role

- support for recovery life-long
- crisis management
- broad knowledge of long term/ late complications
- support and information

management of consequences

- ‘late-effects’ service
- Holistic assessment
- guidelines implementation
- second malignancy screening

reassure patients and care givers

- readmissions common
- complications an expected aspect of recovery
- minority of patients will experience numerous complex readmissions

Motivated self-management

identify the barriers, unlock the potential

tackle behaviour = improve health = reduce LTCs

weight management and nutrition

exercise

alcohol

smoking

work and education

relationships

Reinforce public health messages

- 5-a-day
- alcohol units
- smoking cessation
- exercise
  - 150 minutes of moderate aerobic activity pw
  - strength exercises in two or more days/ pw

brief interventions

oral discussion, negotiation or encouragement

with or without written or other support or follow-up

- may also involve
  - a referral for further interventions such as smoking cessation clinic
  - directing people to other options ie have you thought about trying ….
  - more intensive support such as counselling or therapy
- brief interventions
  - can be delivered by anyone who is trained in the necessary skills and knowledge
  - are often carried out when the opportunity arises, typically taking no more than a few minutes for basic advice
  - **person-centred**

non-adherence

I don't feel ill, why do I need them

I'm afraid of the side effects

I forget

I threw them away

Failure to take the prescribed medication at prescribed time and/ or at the prescribed dose

£m per year is lost due to patients not taking medication properly

One in 5 do not take all their prescribed medication

Tips for improving adherence

- record accurate and current list of medications (prescribed and OTC)
- explore barriers to adherence
- explain aims or benefits of medication
- explore patients health beliefs and their understanding of:
  - their illness
  - the role of medication (s)
  - potential risks of non-adherence
  - side effects
- explore knowledge - provide verbal and written information
- identify whether prompts are needed

Challenges of post transplant recovery

Recovery challenging even in absence of complications

Impact of transplant far-reaching

Long term recovery

- often more challenging than the transplant
- patients feel unprepared
- uncertainty
- unpredictability

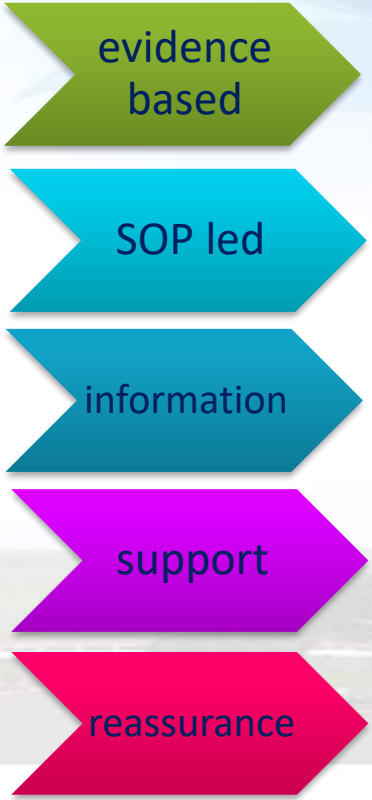
counselling/ psychotherapy often of value

AHP support for rehabilitation

Other support mechanisms

- eg support groups, buddies, mindfulness techniques

Cornerstones of HSCT nursing care



It’s not about winning the race, you just need to cross the line…..

EBMT European Society for Blood and Marrow Transplantation

Thanks!

Any questions?

@TheEBMT_Nurses

michelle.kenyon@nhs.net

ebmt.org

DONORS

Julia Ruiz, Spain

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

INTRODUCTION

- Identify a suitable donor
- Donation is an intense and demanding process
- The choice of donor has an impact on the transplant process.
- Conditions to consider a donor suitable:
  - Needs to be suitably matched
  - Needs to be healthy
  - Willing to donate
- Donors can be related or unrelated and the primary consideration is the degree of HLA compatibility of the donor to the recipient.
  - Possibility of having a suitably matched sibling donor varies depending on ethnicity and family size
  - Possibility of having a suitable matched unrelated donor also varies depending on ethnicity.
  - INCREASE use of alternate donors: **Haploidentical donor, this means that nearly all patients will have a potential donor.**

SUITABLY MATCHED: HLA COMPATIBILITY

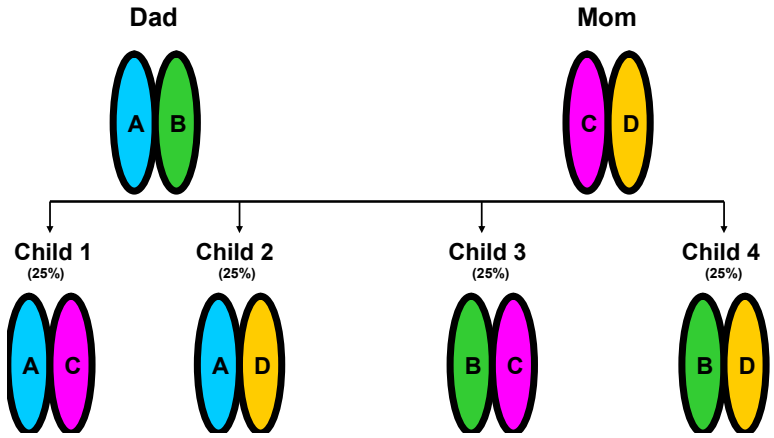
HLA TYPING:

HLA: Human Leukocyte antigen molecules: found in the short arm of chromosome 6.

Wide variety and number of HLA alleles.

Role: Enable T cells to

- Recognise and eliminate “foreign” particles present in an individual
- Prevent the recognition of self as foreign.



INTRODUCTION. RELATED DONOR

RELATED DONOR:

- First option
- THREE IMPORTANT QUESTIONS TO BE DONE BEFORE PROCEEDING:
  - ¿Have you been informed of the donation process?
  - ¿Are you healthy?
  - ¿Are you willing to donate?

- **Syngenic donor** (identical twin)
- **Matched sibling donor**
  - Not always possible: 25%
  - Depends on ethnicity and family size
- **Mismatch related**:
  - Haploidentical donor
  - One, two antigen mismatch.

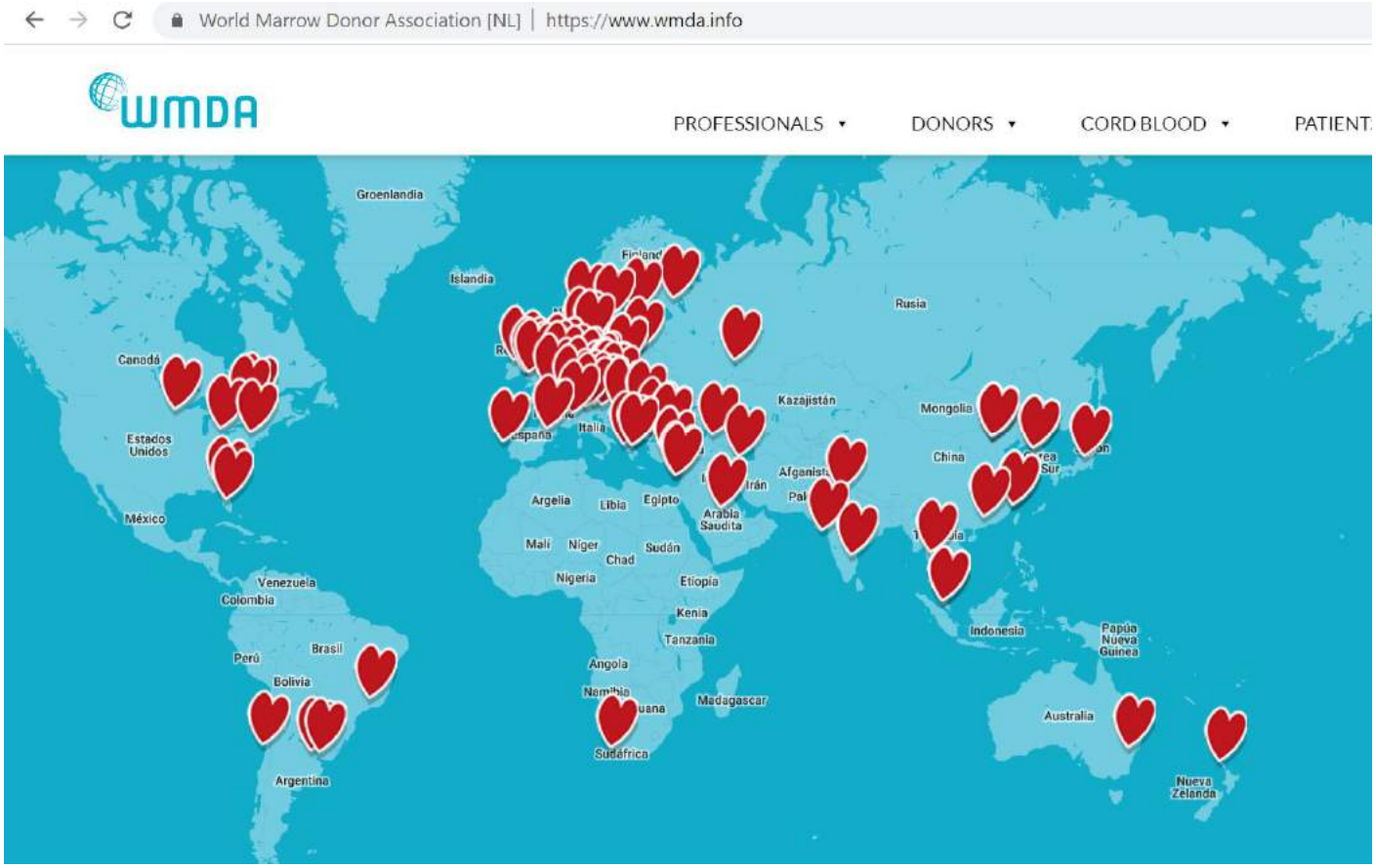
STANDARD:

B6.1.2 *Written criteria shall include criteria for the selection of allogeneic donors when more than one (1) donor is available and suitable.*

B6.1.3 *Information regarding the donation process should be provided, including the considerations for donation, to the potential allogeneic donor prior to HLA typing.*

Sufficient information for allogeneic donors should be provided before the potential donor undergoes HLA typing to protect the potential donor from undue pressure should he/she be the only suitable donor. The Clinical Program may not always have control over the allogeneic donor consent process, but should attempt to provide information to the donor if possible, or review available documentation to verify that the donor received such information.

INTRODUCTION. UNRELATED DONOR



Unrelated donor:

- Registry: BM Donors Worldwide: Takes several weeks, months.
- Cord blood registries: Information available.

INTRODUCTION. UNRELATED DONOR

GeneBandhu New Delhi

Get in contact with the organisation:
Address: 209-C, 2nd and 3rd floor, Masjid Moth
South Extension-II
110049
New Delhi
India

Phone: +91 11 6469 1678

E-mail: patientcare@genebandhu.in

Website: http://dev.genebandhu.in/wordpress/
Social Media: https://www.facebook.com/genebandhu

Do you want to have more information? Please contact the organisation or go to the organisation profile on WMDA Share.

DATRI Blood Stem Cell Donors Registry

Get in contact with the organisation:
Address: Module No.1207 &1208; 12th Floor
TICEL BIO PARK - Phase II, CSIR Road, Taramani
600113
Chennai
India

Phone: +91 442 2541 283

E-mail: raghu@datriworld.org

Website: http://datri.org
Social Media: https://www.facebook.com/datriworld

Do you want to have more information? Please contact the organisation or go to the organisation profile on WMDA Share.

MDR Marrow Donor Registry India Mumbai

Get in contact with the organisation:
Address: Raheja/Fortis Hospital, 2nd Floor
Old Wing, Mahim
400016
Mumbai
India

Phone: +91 226 5152 695

E-mail: sunil@parekh.net.in

Website: http://mdrindia.org
Social Media: https://www.facebook.com/friendsofmdri

Do you want to have more information? Please contact the organisation or go to the organisation profile on WMDA Share.

Gift of life: Have you registered on the stem cells donors list?

Donating stem cells to save a life is now a painless, non-invasive process. It's as simple as donating blood. And non-profit registries across India are doing what they can to popularise the idea

HEALTH Updated: Feb 24, 2018 19:05 IST

Anonna Dutt and Anesha George
Hindustan Times

Data from DATRI's database shows that the highest numbers of registered donors are from southern states of India. Kerala takes the lead with 60,630 registrations. Registrations are much lower in Chandigarh (883), Rajasthan (1,158), Punjab (3,468), and Haryana (4,816). Nearly 6,000 donors from Delhi are registered with DATRI.
"Only 10% of the people who need a bone marrow transplant manage to find a match. Every month we get a request for nearly 200 matches, but we are able to get a donor for only 12 or 15 people," says Raghu Rajagopal, DATRI's co-founder and CEO.

INTRODUCTION. UNRELATED DONOR

Table 3.3 Likelihood of identifying HLA-matched adult donors and cord blood units

U.S. Racial and Ethnic Group	Likelihood of identifying an adult donor[a]		Likelihood of identifying a cord-blood unit for patients ≥20 Yr of age[b]			Likelihood of identifying a cord-blood unit for patients <20 Yr of age?		
	8/8 HLA match	≥7.8 HLA match	6/6 HLA match	≥5/6 HLA match	≥4/6 HLA match	6/6 HLA match	≥5/6 HLA match	≥4/6 HLA match
				Percent				
White European	75	97	17	66	96	38	87	99
Middle Eastern or North African	46	90	6	46	91	18	75	98
African American	19	76	2	24	81	6	58	95
African	18	71	1	23	81	5	56	95
Black South or Central American	16	66	2	27	82	7	58	96
Black Caribbean	19	74	1	24	81	6	58	95
Chinese	41	88	6	44	91	19	77	98
Korean	40	87	5	39	89	17	73	98
South Asian	33	84	4	41	90	14	73	98
Japanese	37	87	4	37	88	16	72	97
Filipino	40	83	5	42	89	19	76	98
Southeast Asian	27	76	3	37	89	12	70	98
Vietnarnese	42	84	6	44	89	20	76	98
Hawaiian or Pacific Islander	27	72	3	32	84	10	64	96
Mexican	37	87	6	45	91	19	75	98
Hispanic South or Central American	34	80	5	43	90	17	73	98
Hispanic Caribbean	40	83	5	40	89	17	71	98
Native North American	52	91	10	54	93	25	80	99
Native South or Central American	49	87	11	53	93	26	79	98
Native Caribbean	32	77	4	35	86	14	66	97
Native Alaskan	36	83	7	47	91	18	75	98

Gragert et al. 2014

[a]Data are the probabilities of identifying an adult donor who is available

[b]Data are the probabilities of identifying a unit with an adequate cell dose

INTRODUCTION. TREND DONORS

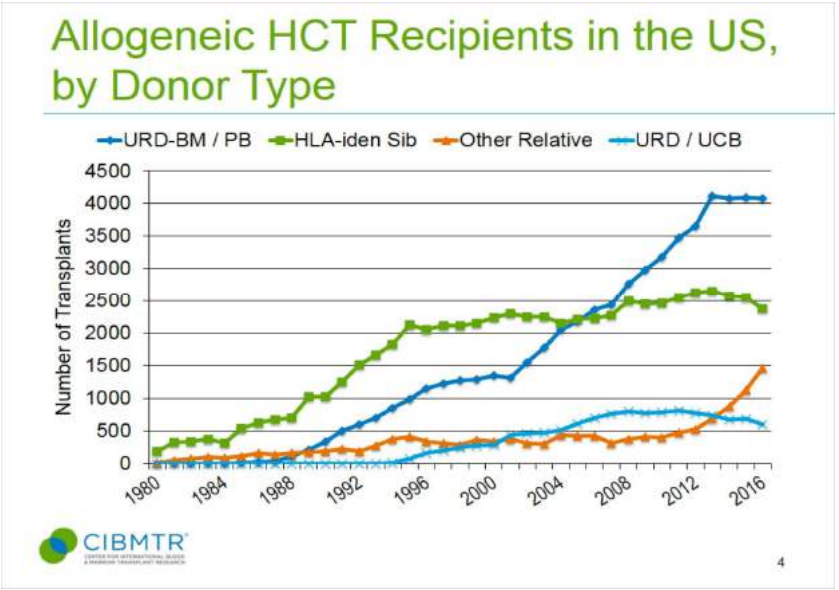
Bone Marrow Transplantation (2018) 53:1139–1148
https://doi.org/10.1038/s41409-018-0153-1

ARTICLE

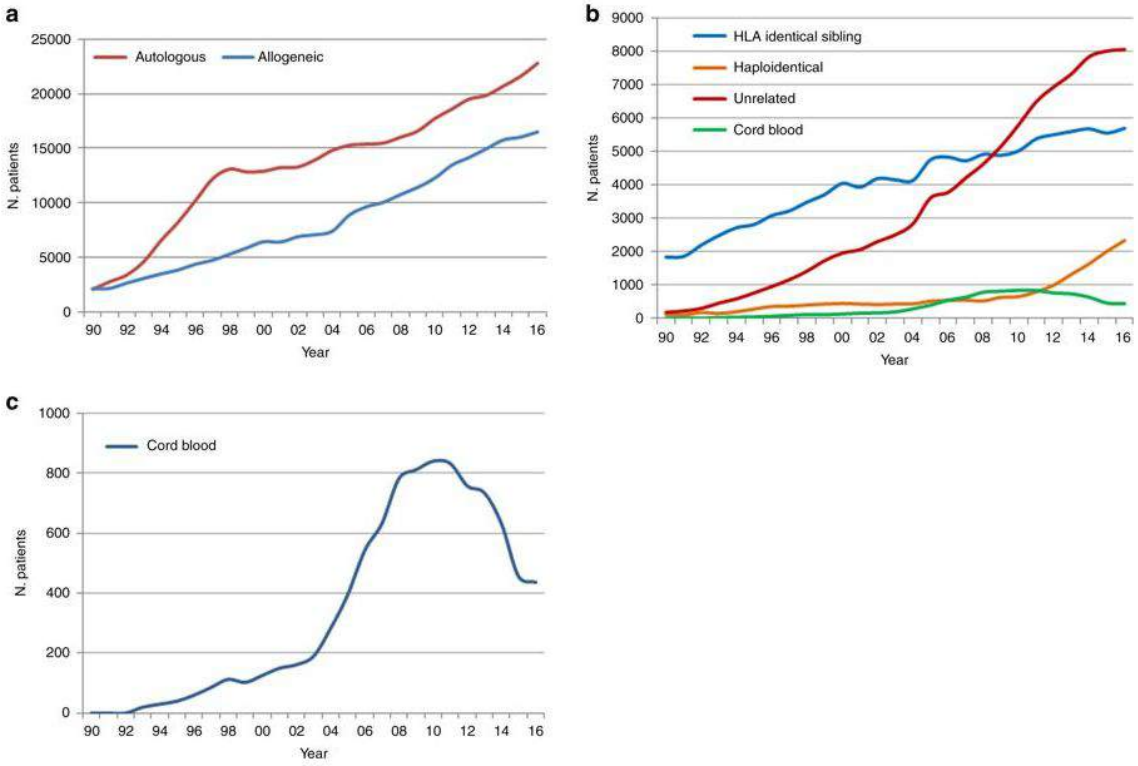
Is the use of unrelated donor transplantation leveling off in Europe? The 2016 European Society for Blood and Marrow Transplant activity survey report

Jakob R Passweg[1] · Helen Baldomero[1] · Peter Bader[2] · Grzegorz W. Basak[3] · Chiara Bonini[4] · Rafael Duarte[5] · Carlo Dufour[6] · Nicolaus Kröger[7] · Jürgen Kuball[8] · Arjan Lankester[9] · Silvia Montoto[10] · Arnon Nagler[11] · John A. Snowden[12] · Jan Styczynski[13] · Mohamad Mohty[14] for the European Society for Blood and Marrow Transplantation (EBMT)

Received: 14 December 2017 / Revised: 30 January 2018 / Accepted: 7 February 2018 / Published online: 14 March 2018



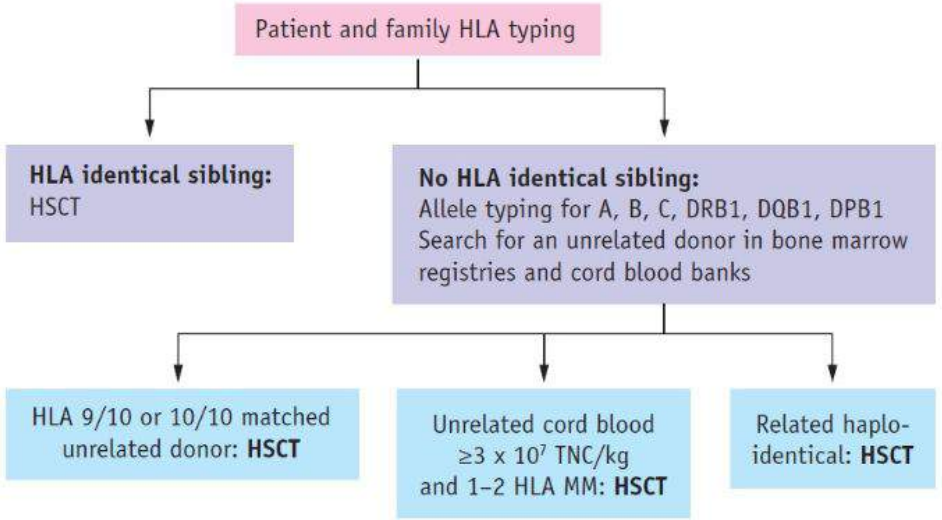
From: Is the use of unrelated donor transplantation leveling off in Europe? The 2016 European Society for Blood and Marrow Transplant activity survey report



Trend in the absolute numbers of HCT in Europe 1990–2016. **a** Trend in allogeneic and autologous HCT. **b** Changes in donor choice. **c** Trend in cord blood HCT

INDICATIONS. DONOR SELECTION

Figure 4: **Algorithm of donor search**



- If transplant urgent: prefer cord blood or related haploidentical transplant
- If not enough cells in a single cord blood unit: consider double cord
- Consider other factors: indication of the transplant, ABO, CMV, donor sex
- Expertise of the centres is very important for donor selection for HLA mismatched transplants

INDICATIONS. DONOR ELIGIBILITY

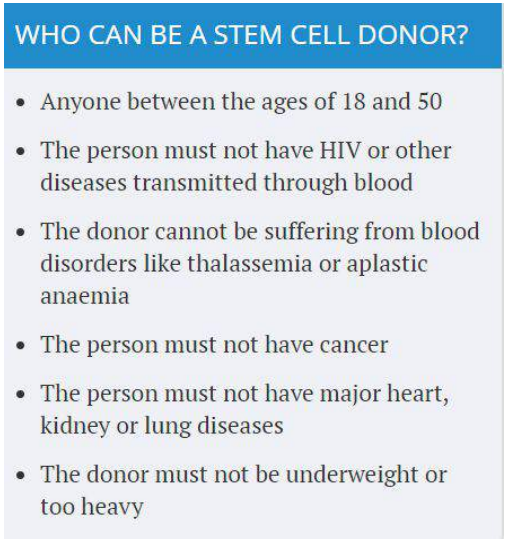
Exclusion criteria for related donors

Own requirements of institution and regulations:

- Potential donor not a risk for recipient
- Potential donor not a risk for themselves
- Previous malignancy or autoinmune condition

Exclusion criteria for unrelated donors:

Each registry will have their criteria



WHO CAN BE A STEM CELL DONOR?

- Anyone between the ages of 18 and 50
- The person must not have HIV or other diseases transmitted through blood
- The donor cannot be suffering from blood disorders like thalassemia or aplastic anaemia
- The person must not have cancer
- The person must not have major heart, kidney or lung diseases
- The donor must not be underweight or too heavy

INDICATIONS. DONOR ELIGIBILITY

CMV STATUS:

Should be matched donor-recipient.

- Recipient CMV+ ⟶ Donor CMV+ or CMV-
- Recipient CMV- ⟶ Donor CMV-

CMV is a common virus but it is a concern for immunosuppressed patients if developing CMV infection.

BLOOD GROUP:

Mismatch is not a contraindication.

Important consideration if bone marrow product is selected

It must be red cell depleted to avoid hemolytic reactions.

SEX MATCH:

Important predictor of transplant-related mortality

Male recipient with female donor

- Increased risk of chronic GVHD
- Higher transplant realted mortality (TMR)

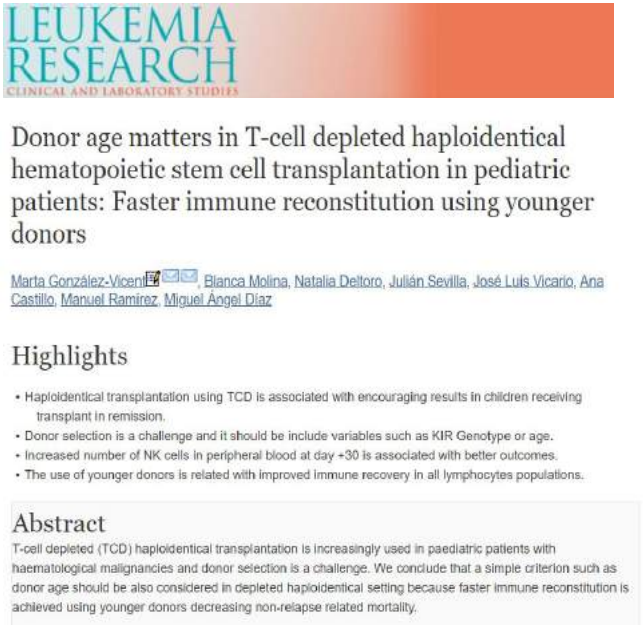
INDICATIONS. DONOR ELIGIBILITY

PARITY:

- Non parous
- Parous:
  - HLA-specific antibodies due to exposure to foetal antigens in utero.
  - Major risk fo chronic GVHD.

AGE:

- Younger age better outcome after transplant.
- Increased age: risk of acute GVHD, chronic GVHD is higher and survival can be lower.



LEUKEMIA RESEARCH
CLINICAL AND LABORATORY STUDIES

Donor age matters in T-cell depleted haploidentical hematopoietic stem cell transplantation in pediatric patients: Faster immune reconstitution using younger donors

Marta González-Vicent, Blanca Molina, Natalia Deltoro, Julián Sevilla, José Luis Vicario, Ana Castillo, Manuel Ramírez, Miguel Ángel Díaz

Highlights

- Haploidentical transplantation using TCD is associated with encouraging results in children receiving transplant in remission.
- Donor selection is a challenge and it should be include variables such as KIR Genotype or age.
- Increased number of NK cells in peripheral blood at day +30 is associated with better outcomes.
- The use of younger donors is related with improved immune recovery in all lymphocytes populations.

Abstract

T-cell depleted (TCD) haploidentical transplantation is increasingly used in paediatric patients with haematological malignancies and donor selection is a challenge. We conclude that a simple criterion such as donor age should be also considered in depleted haploidentical setting because faster immune reconstitution is achieved using younger donors decreasing non-relapse related mortality.

INDICATIONS. DONOR ELIGIBILITY JACIE

EVALUATION:

SIMPLE PRINCIPLE: “First, do no harm”

- *B6.1 There shall be written criteria for allogeneic and autologous donor selection, evaluation, and management by trained medical personnel.*
- *B6.3.1.2 Allogeneic donor suitability shall be evaluated by a licensed health care professional who is not the primary health care professional overseeing care of the recipient.*

MEDICAL HISTORY:

- Vaccination history.
- Travel history.
- Blood transfusion history.
- Questions to identify persons at high risk for transmission of communicable disease as defined by the applicable governmental authority.
- Questions to identify persons at risk of transmitting inherited conditions.
- Questions to identify persons at risk of transmitting a hematological or immunological disease.
- Questions to identify a past history of malignant disease.
- The allogeneic donor shall confirm that all the information provided is true to the best of his/her knowledge.

Table 3.4 Pre-transplant investigations of the donor

Blood group and antibody screening
Coagulation studies
Complete blood count
Full/confirmatory HLA typing
Liver function tests
Urea and creatinine
Pregnancy test
Viral serology – Cytomegalovirus Epstein-Barr virus Hepatitis B surface antigen and core antibody Hepatitis C antigen HIV HTLV Treponemel screen Herpes simplex virus Varicella zoster virus Toxoplasma
Chest X-ray
Electrocardiogram
Under certain circumstances
Cytogenetic studies (chromosome fragility) if family history
Bone marrow examination
Echocardiogram or MUGA scan
Haemoglobin electrophoresis
Lung function tests
Haemoglobinopathy screen

INDICATIONS. DONOR CONSENT JACIE

CONSENT: Written consent prior to starting conditioning of recipient

B6.2; C6.2; CM6.2	ALLOGENEIC AND AUTOLOGOUS DONOR INFORMATION AND CONSENT TO DONATE / FOR COLLECTION
B6.2.1; C6.2.1; CM6.2.1	The collection procedure shall be explained in terms the donor can understand, and shall include the following information at a minimum:
B6.2.1.1; C6.2.1.1; CM6.2.1.1	The risks and benefits of the procedure.
B6.2.1.2; C6.2.1.2; CM6.2.1.2	Tests and procedures performed on the donor to protect the health of the donor and the recipient.
B6.2.1.3; C6.2.1.3; CM6.2.1.3	The rights of the donor or legally authorized representative to review the results of such tests according to applicable laws and regulations.
B6.2.1.4	Alternative collection methods.
B6.2.1.5; C6.2.1.4; CM6.2.1.4	Protection of medical information and confidentiality.
B6.2.4; C6.2.4; CM6.2.4	The donor shall have an opportunity to ask questions.
B6.2.5; C6.2.5; CM6.2.5	The donor shall have the right to refuse to donate or withdraw consent.
B6.2.5.1; C6.2.5.1; CM6.2.5.1	The allogeneic donor shall be informed of the potential consequences to the recipient of such refusal in the event that consent is withdrawn after the recipient begins the preparative regimen.

INDICATIONS. ELDER/PEDIATRIC JACIE

B6.1.1 Written criteria shall include criteria for the selection of allogeneic donors who are minors or older donors.

ELDER:

- Age-related medical conditions
- Additional tests to reduce risk donor

PEDIATRIC:

B6.4.1 A donor advocate shall be available to represent allogeneic donors who are minors or who are mentally incapacitated, as those terms are defined by applicable laws.

- 600-700 become hematopoietic stem cell donors for their siblings every year

DONOR ADVOCATE:

- Help parents weigh risks and benefits for the healthy child
- Role:
  - Training potential psychological and physical consequences of donation
  - Understanding the ethical and legal basis of voluntary donation
  - Independence from conflicts of interest


Biol Blood Marrow Transplant 22 (2016) 96–103

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Clinical Research: Pediatric

Determination of Eligibility in Related Pediatric Hematopoietic Cell Donors: Ethical and Clinical Considerations. Recommendations from a Working Group of the Worldwide Network for Blood and Marrow Transplantation Association

Menachem Bitan [1,*], Suzanna M. van Walraven [2], Nina Worel [3], Lynne M. Ball [2], Jan Styczynski [4], Marta Torrabadella [5], Volker Witt [6], Bronwen E. Shaw [7], Adriana Seber [8], Hiromasa Yabe [9], Hildegard T. Greinix [10], Christina Peters [6], Eliane Gluckman [11], Vanderson Rocha [12], Joerg Halter [13], Michael A. Pulsipher [14]

EVIDENCE BASED PRACTICE. DONOR FOLLOW-UP

- WMDA encourages internal data collection on donor complications both during and following donation.
- A donor follow-up is recommended 30 days after collection, and then one year, five years and 10 years after donation.
- Data on related donors are scarce
- Theoretical concerns about long-term effects after donation have not been verified yet
- Numbers of donors lost to follow-up remain a problem

SPECIAL REPORT

Allogeneic hematopoietic stem cell donation—standardized assessment of donor outcome data: A consensus statement from the Worldwide Network for Blood and Marrow Transplantation (WBMT)

JP Halter[1], SM van Walraven[2], N Worel[3], M Bengtsson[4], H Hägglund[5], G Nicoloso de Faveri[6], BE Shaw[7], AH Schmidt[8], M Fechter[9], A Madrigal[10], J Szer[11], MD Aljurf[12], D Weisdorf[13], MM Horowitz[14], H Greinix[15], D Niederwieser[16], A Gratwohl[1], Y Kodera[17] and D Confer[18]

Bone Marrow Transplantation (2013) 48, 220–225

Table 2. Minimal data set to be reported after the end of the donation procedure

Time interval covered: start of donation procedure until day 30 after completion of the procedure
Time of report: between day 30 and day 100 after the donation procedure

Donor data
- Donor ID[a]
- Age at donation
- Sex
- Relationship to the recipient:
  - Twin
  - Sibling
  - Other family member
  - Unrelated donor

Collection data
- Start date of the procedure
- Was the product collection completed?
  - Yes/no
- Number of collections/subsequent donations
- Were hematopoietic growth factors used (for example, G-CSF)?[b]
  - Yes/no
- Were cell binding inhibitors used (for example, plerixafor)?[b]
  - Yes/no
- Was EPO used?[b]
  - Yes/no
- Were other drugs used for mobilization?
  - Yes/no (without further specification)

Product
- BM (including collection of MSC)
- PBSC
- Both (BM and PBSC)
- Unstimulated leukapheresis (for example, DLI)
- Others

Complications in temporal association with the donation procedure
- Report only serious adverse reactions (SAE/R) with International Classification of Diseases (ICD)10 coding (a list with a selection of the anticipated most frequent events is available in Supplementary Information)
- Report every SAE/R occurring within the interval between start of the donation procedure and day 30 after end of the donation procedure

INDICATIONS. SOURCE HSC

- Source selection: dictated by the transplant medical assessment and the type of transplant
  - Donor has a choice in which type of donation method they prefer.
  - Medical issue of the donor
  - Adequate peripheral venous access.
- It is known that using PBSC gives more GvHD which is favourable in malignant diseases where increasing GvHD decreases the risk of relapse while in non-malignant diseases, especially in aplastic anaemia, it decreases survival.

CONCLUSION

- Nearly all patients will have a potential donor.
- Promote volunteer bone marrow donors.
- Conditions to consider a donor suitable:
  - Needs to be suitably matched
  - Needs to be healthy
  - Willing to donate
- Donor must be evaluated by an independent professional different from patient.
- Confidentiality of donor issues.
- Donor must have a scheduled follow-up.

Literature reference

- ONS Hematopoietic Stem Cell Transplantation. Manual for nurse practice
- EBMT Handbook. Haematopoietic Stem Transplantation. Springer
- EBMT Textbook for Nurses. Springer
- Pediatric Oncology nursing. Springer
- Kisch, AM. Allogeneic stem cell transplant. Patient and sibling donors perspective. Malmo University. 2015.
- Donor age matters in T-cell depleted haploidentical hematopoietic stem cell transplantation in pediatric patients: Faster immune reconstitution using younger donors. Leukemia Research.Marta González-Vicent et al.

BLOOD TRANFUSION
ABO INCOMPATIBILITY

Julia Ruiz, Spain

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

INTRODUCTION

Transplanted patients often require intensive blood component support, during aplasia.

- Local and national policies for high quality and appropiate transfusión.
- Policies and procedures regularly audited

DONORS:

- May be scarce….need donors
- Easy
- No risk
- Components:
  - Red cells
  - Platelets
  - Plasma (frozen)
  - Granulocyte

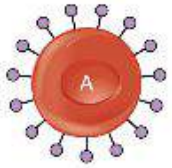
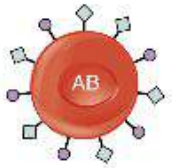
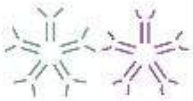
ERITHROCYTES are administered in severe anemia

PLATELETS are administered to correct thrombocytopenia to prevent o r treat bleeding

PLASMA is administered to help correct coagulation factors.

INTRODUCTION. ABO Rh groups

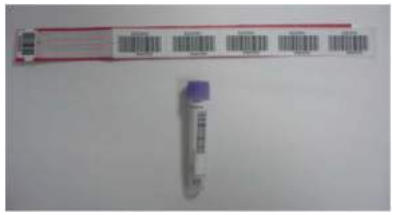
- **ABO incompatibilities** when RBC antigens andantibodies between the donor and the recipient are mismatched.
- **Immune response**: destruction of the cell.
- UNIVERSAL DONOR: 0 NEG.

	A	B	AB	O
Red Blood Cell Type				
Antibodies in Plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in Red blood Cell	 A antigen	 B antigen	 A and B antigens	None
Blood Types Compatible in an Emergency	A, O	B, O	A, B, AB, O (AB^+ is the universal recipient)	O (O is the universal donor)

Blood type	Erythrocyte antigens (agglutinogens)	Serum antibodies (isoagglutins)	Compatible RBC type	Can receive blood from
AB	A and B	None	AB	AB, A, B, O
A	A	B	A and AB	A and O
B	B	A	B and AB	B and O
O	None	A and B	AB, A, B, O	O

INDICATIONS. TRANSFUSION

- Accurate collection of pretransfusion blood samples for typing and crossmatching.
- Some facilities may require a second authorized staff member to witness and sign the form

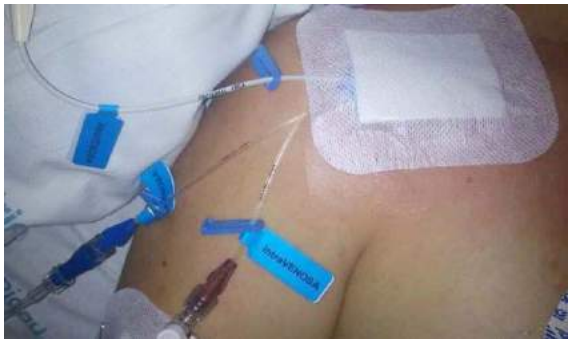


BEFORE TRANSFUSION:

- Verify that an order for the transfusion exists.
- Physical assessment of the patient (including vital signs) to help identify later changes.
- Document your findings: obtain the patient's vital signs **before, during, and after the transfusion.**

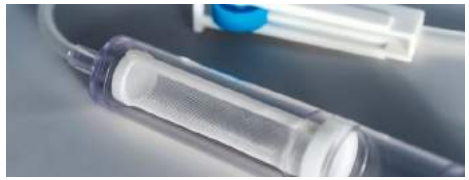
INDICATIONS. TRANSFUSION

- Confirm that the patient has given informed consent.
- Teach the patient about the procedure's associated risks and benefits, what to expect during the transfusion, signs and symptoms of a reaction, and when and how to call for assistance.
- Check for an appropriate vascular access.



- Equipment at hand for administering the blood product and managing a reaction, such as an additional free I.V. line for normal saline solution, oxygen, suction, and a hypersensitivity kit.
- Specific product to be transfused: the appropriate administration rate, and required patient monitoring.

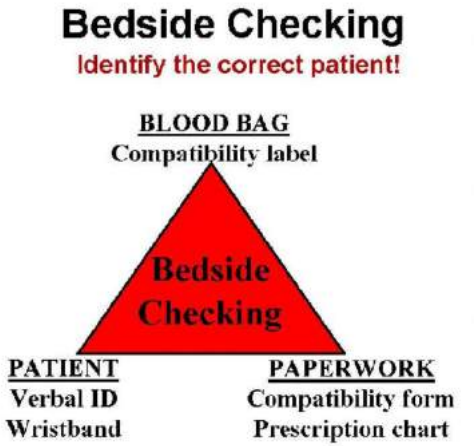
INDICATIONS. TRANSFUSION

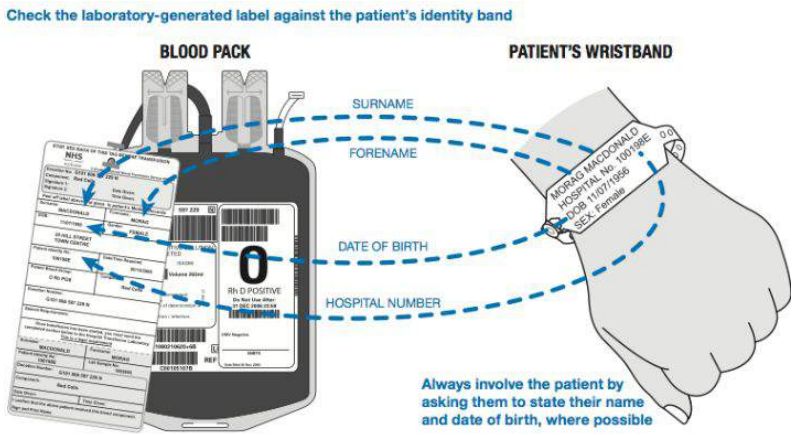


- **RBC:**
  - Requires crossmatching within 72 hours.
  - ABO identical and Rh compatible
  - Transfuse time, maximum 4 hours from refrigerator removal (risk of bacterial growth)
  - Initial low rate, first 15 min or first 50 ml volume
  - Infusion through filter
- **Platelets:**
  - ABO and Rh compatibility recommended.
  - Infusion rapidly (20-60 minutes) through filter (170mm diameter filter)
- **Fresh frozen plasma**:
  - Crossmatching not required, ABO-compatible
  - Infusion over 2-4 hours within 6 hours of thaw time.

INDICATIONS. TRANSFUSION

- Personnel available: physician and blood bank representative. Contact if adverse event.
- Double-check the patient's identification and verify the actual product.
- Check the unit to be transfused against patient identifiers





- Start infusion of blood product.
- Document when finalized.

INDICATIONS. ABO INCOMPATIBILITY

B6.4.3 Allogeneic donors and allogeneic recipients shall be tested for ABO group and Rh type using two independently collected samples. Discrepancies shall be resolved and documented prior to issue of the cellular therapy product.

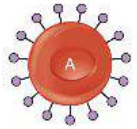
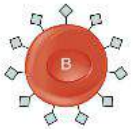
INDICATIONS. ABO INCOMPATIBILITY

MAJOR INCOMPATIBILITY:

Donor with incompatible red cell *antigen*, such as group A donor and group O recipient, so RBCs in HPC are hemolyzed during infusion

a) Group O recipients receiving non-O (A,B,AB) HPCs

b) Group non-AB(O,A,B) recipientes receiving AB HPCs

	A	B	AB	O
Red Blood Cell Type				
Antibodies in Plasma	Anti-B	Anti-A	RECIPIENT None	Anti-A and Anti-B
Antigens in Red blood Cell DONOR	A antigen	B antigen	A and B antigens	None
Blood Types Compatible in an Emergency	A, O	B, O	A, B, AB, O (AB+ is the universal recipient)	O (O is the universal donor)

HPC Donor

HPC Recipient	O	A	B	AB
O	✓	Major	Major	Major
A	Minor	✓	Both	Major
B	Minor	Both	✓	Major
AB	Minor	Minor	Minor	✓

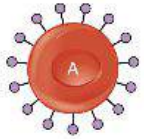
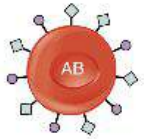
INDICATIONS. ABO INCOMPATIBILITY

MINOR INCOMPATIBILITY

Donor with incompatible red cell *antibody*, such as group O donor and group A recipient, so recipient RBCs are hemolyzed during infusion

a) Group AB recipients receiving non-AB (O,A,B) HPCs

b) Group non-O (A,B,AB) recipients receiving O HPCs

	A	B	AB	O
Red Blood Cell Type				
Antibodies in Plasma	Anti-B	Anti-A	None	Anti-A and Anti-B
Antigens in Red blood Cell RECIPIENT	A antigen	B antigen	A and B antigens	None
Blood Types Compatible in an Emergency	A, O	B, O	A, B, AB, O (AB^+ is the universal recipient)	O (O is the universal donor)

DONOR

HPC Recipient \ HPC Donor	O	A	B	AB
O	✓	Major	Major	Major
A	Minor	✓	Both	Major
B	Minor	Both	✓	Major
AB	Minor	Minor	Minor	✓

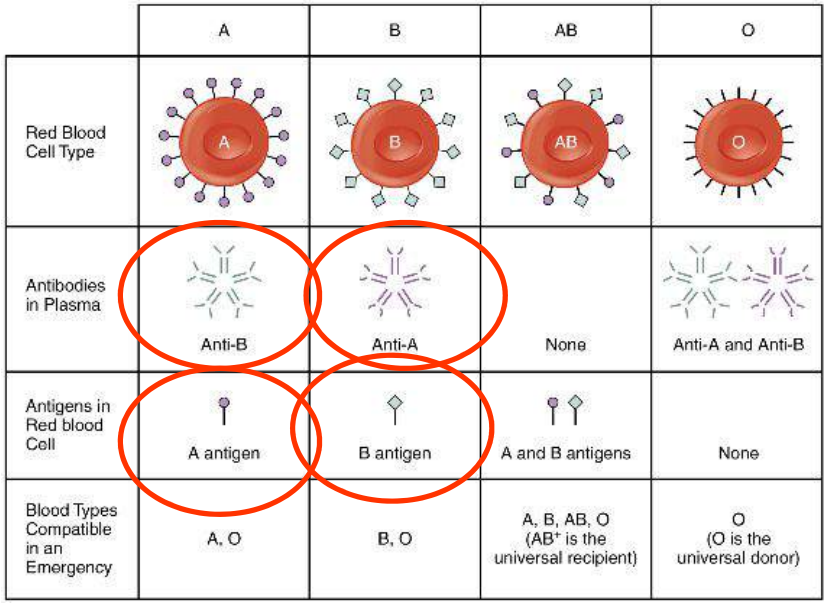
INDICATIONS. ABO INCOMPATIBILITY

BIDIRECTIONAL INCOMPATIBILITY:

Donor *antigens and antibodies* incompatible with recipient; so both donor and recipient RBCs may be hemolyzed during infusion

a) Group A donor/group B recipient

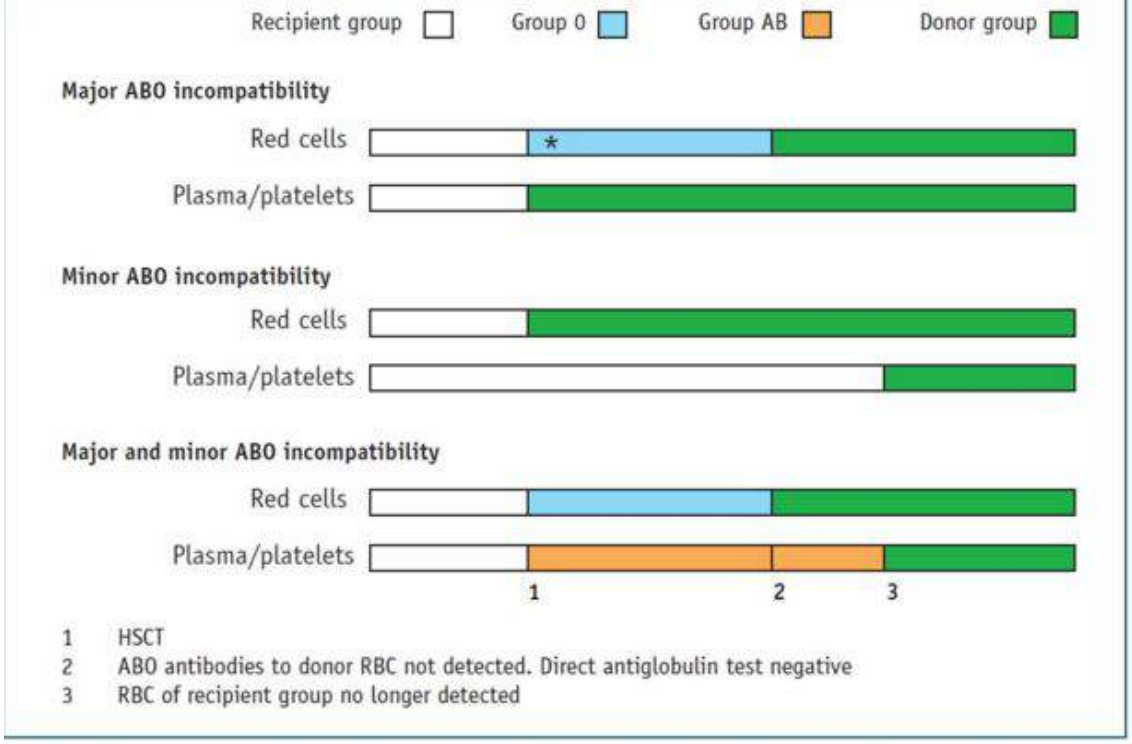
b) Group B donor/group A recipient



HPC Recipient \ HPC Donor	O	A	B	AB
O	✓	Major	Major	Major
A	Minor	✓	Both	Major
B	Minor	Both	✓	Major
AB	Minor	Minor	Minor	✓

INDICATIONS. ABO INCOMPATIBILITY

Figure 1: **Strategy for the provision of blood components in ABO mismatched HSCT**



**Or recipient-type red cells. Modified from Practical Transfusion Medicine with permission (Figure 27.3, page 138). Practical Transfusion Medicine (Third Edition) Murphy MF, Pamphilon D, Wiley-Blackwell Publishers 2009; 138*

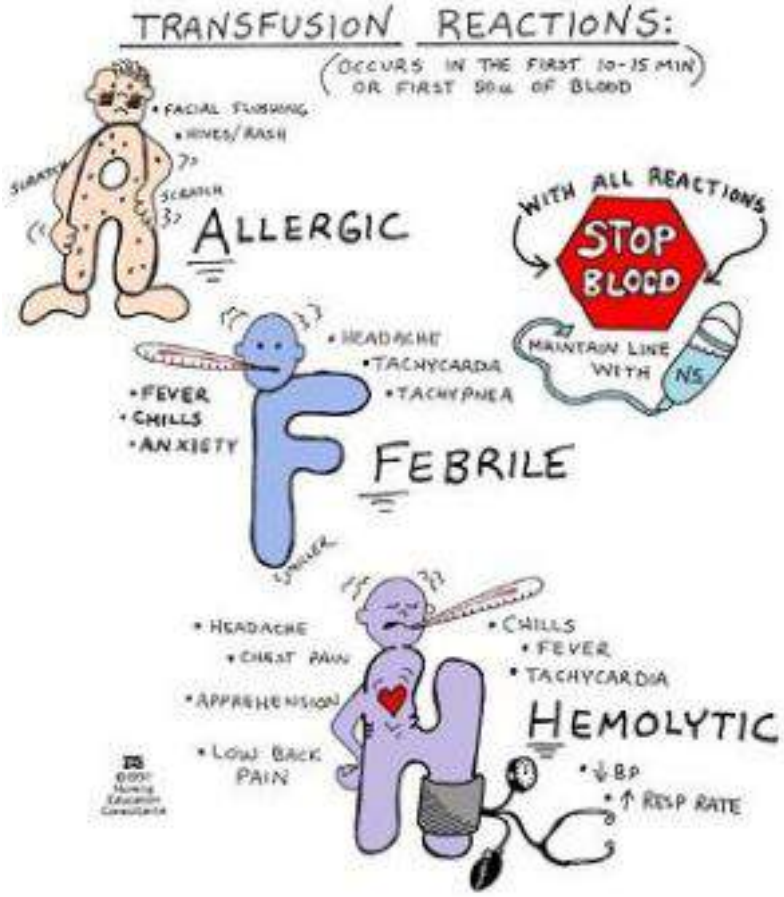
INDICATIONS. ABO INCOMPATIBILITY

Recipient group after tansplant will change to donor group.

- PRE-TRANSPLANT: blood component support should be with recipient type blood components.
- POST-TRANSPLANT: The following groups should be given post-transplant until engraftment when ABO antibodies to the donor ABO group are undetectable and the direct antiglobulin test is negative:
- *Major ABO incompatibility*: red cells of group O or recipient's own ABO group should be given. Plasma and platelets should be of donor-type blood group.
- *Minor ABO incompatibility*: red cells of donor ABO group should be given. Plasma and platelets should be of recipient-type blood group.
- *Bidirectional ABO incompatibility*: give group O red cells, group AB plasma and platelets of recipient-type blood group.

INDICATIONS. TRANSFUSION REACTION

- Transfusion reactions may ocurr during and up to several hours after transfusion
- STOP the transfusion.
- Keep the I.V. line open with normal saline solution.
- Notify the physician and blood bank.
- Treatment for signs and symptoms as appropriate.
- Monitor the patient's vital signs.
- Return the blood product to the blood bank and collect laboratory samples according to facility policy.
- Document transfusion-related events according to facility policy; include the patient's vital signs, other assessment findings, and nursing interventions.



INDICATIONS. TRANSFUSION REACTION

HEMOLYTIC REACTION

- Incompatibility between transfused donor RBC and recipient alloantibodies.
- Acute intravascular hemolysis and extravascular RBC destruction
- Usually appear within the first 5-15 minutes after transfusion is started.
  - Temperature increase, chills
  - Hemoglobinuria
  - Hypotension
  - Sever low back pain or chest pain
  - Anuria
  - Nausea and vomiting
  - Dyspnea, wheezing
  - Anxiety
  - Generalized bleeding
  - **STOP + antihistamine, antipyretic + hydrate with saline solution + vital signs**

INDICATIONS. TRANSFUSION REACTION

- **NONHEMOLYTIC REACTIONS**
  - More common
  - Symptoms:
    - Chills
    - Fever
    - Urticaria
    - Rigors
    - Headache
    - Nauseas
  - **STOP + antihistamime + antipyretic**
  - **Premedication future transfusion**

INDICATIONS. TRANSFUSION REACTION

ALLERGIC REACTIONS

- Allergens found in plasma may cause allergic transfusion reaction. If the recipient is sensitive to these, antibodies will be produced.
- Symptoms
    - Skin erithema
    - Pruritis
    - Swollen lips
    - Vomiting
    - Hypotension
    - Wheezing
    - Laryngeal edema
    - Anxiety
    - Irritabiity
    - Progression to anaphylaxis
- **STOP + antihistamine and esteroide**

CONCLUSION

- Special consideration and carefully defined policies to minimise adverse effects:
- Use of high quality blood components which have a high degree of microbiological safety.
- Blood grouping (Incompatibility recipient-donor)
- Irradiation of blood products (conditioning until 6 months post-transplant)
- Leukodepleted products
- CMV seronegative products

THANK YOU FOR YOUR ATTENTION.

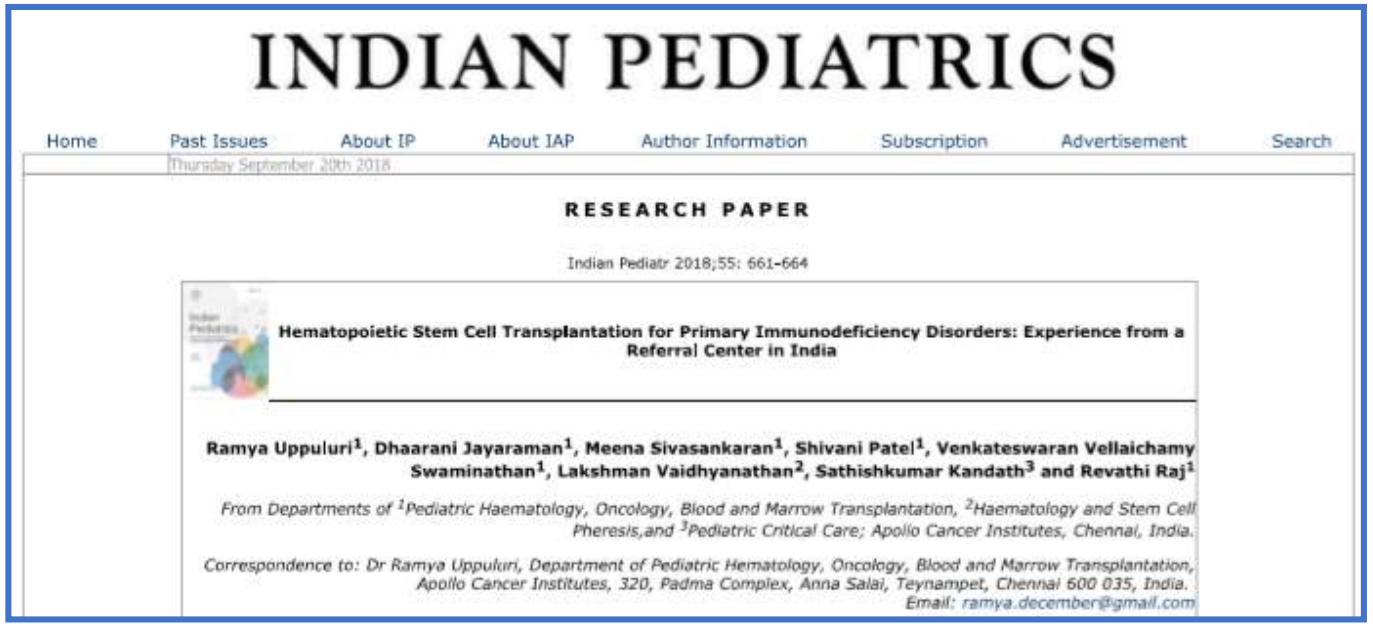
Management of pediatric recipients – clinical case presentations

Eugenia Trigoso. Spain

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

Background & Introduction



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Thursday September 20th 2018

RESEARCH PAPER

Indian Pediatr 2018;55: 661-664

Hematopoietic Stem Cell Transplantation for Primary Immunodeficiency Disorders: Experience from a Referral Center in India

Ramya Uppuluri[1], Dhaarani Jayaraman[1], Meena Sivasankaran[1], Shivani Patel[1], Venkateswaran Vellaichamy Swaminathan[1], Lakshman Vaidhyanathan[2], Sathishkumar Kandath[3] and Revathi Raj[1]

From Departments of [1]Pediatric Haematology, Oncology, Blood and Marrow Transplantation, [2]Haematology and Stem Cell Pheresis,and [3]Pediatric Critical Care; Apollo Cancer Institutes, Chennai, India.

Correspondence to: Dr Ramya Uppuluri, Department of Pediatric Hematology, Oncology, Blood and Marrow Transplantation, Apollo Cancer Institutes, 320, Padma Complex, Anna Salai, Teynampet, Chennai 600 035, India. Email: ramya.december@gmail.com

Primary immunodeficiency disorders (PID) are inherited disorders with impaired and dysregulated immunity characterised by recurrent infections, failure to thrive and a propensity for malignancy, especially lymphoma. Hematopoietic stem cell transplantation (HSCT) is a curative option available with intact survival post- HSCT. HSCT in PID can be challenging due to associated co-morbidities and underlying immune dysregulation.

PID are common in India due to a high incidence of consanguineous marriages. There is a paucity of data from India with recent studies reporting an incidence of more than one per million [1,2]. The lack of early diagnosis, awareness and late referral for HSCT are likely contributory factors to the hitherto poor outcome in these children [3].

Background & Introduction

Med Clin (Barc). 2018 Jul 9. pii: S0025-7753(18)30333-6. doi: 10.1016/j.medcli.2018.05.013. [Epub ahead of print]

Haematopoietic stem cell transplantation in paediatric patients with β-thalassaemia and sickle cell disease: An experience of the Spanish Working Group for Bone Marrow Transplantation in Children (GETMON).

[Article in English, Spanish]
Alonso L[1], González-Vicent M[2], Belendez C[3], Badell I[4], Sastre A[5], Rodríguez-Villa A[6], Bermúdez-Cortés M[7], Hladun R[8], Díaz de Heredia C[8].

BACKGROUND AND OBJECTIVES: A recently occurring increase of the prevalence of haemoglobinopathies, β-thalassaemia major (TM) and sickle cell disease (SCD) over the last two decades in our country has generated new needs in terms of medical resources for both prevention and treatment of these patients. Allogeneic haematopoietic stem cell transplant (allo-HSCT) is a curative treatment available for patients who

-HSCT in paediatric patients wi

arrow Transplantation in Children (G

Allogeneic haematopoietic stem cell transplant (allo-HSCT) is a curative treatment available for patients who have severe haemoglobinopathies.

Background & Introduction

Clinical case presentations

- PATIENT:
  Gender: Male
  Age: 8 years old
- Diagnosis: Thalassemia major
  Original : Paquistan
- Date of diagnosis: 18-09-2010
- At transplant, transfusion dependant: every 3-4 weeks.
  Iron chelation : Deferasirox (Exjade)
- Transplant indicated
- Date of transplant : 28-02-2018
- Donor: Mother haploidentical
  HLA: 9/10
  HLA-A: 1 diference

Background & Introduction

An Pediatr (Barc). 2013 Aug;79(2):75-82. doi: 10.1016/j.anpedi.2012.12.002. Epub 2013 Feb 9.

[Results of hematopoietic stem cell transplantation in hemoglobinopathies: thalassemia major and sickle cell disease].

[Article in Spanish]

Hladun R[1], Elorza I, Olivé T, Dapena JL, Llort A, Sánchez de Toledo J, Díaz de Heredia C.

Author information

Abstract

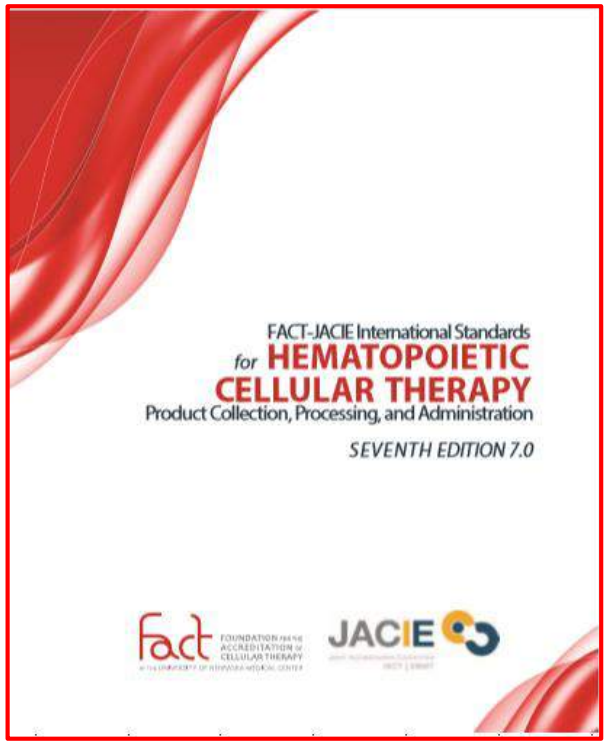
BACKGROUND: The prevalence of hemoglobinopathies in Spain is increasing as a result of immigration. Thalassemia major presents with chronic hemolytic anemia that requires regular red blood cell transfusions within the first year of life. Patients with sickle cell disease suffer from chronic anemia, vasculopathy and progressive damage in almost any organ. There is decreased life expectancy in both conditions. Allogeneic hematopoietic stem cell transplantation represents the only potentially curative option.

Thalassemia major presents with chronic hemolytic anemia that requires regular red blood cell transfusions within the first year of life.. Allogeneic hematopoietic stem cell transplantation represents the only potentially curative option.

Background & Introduction

Clinical case presentations

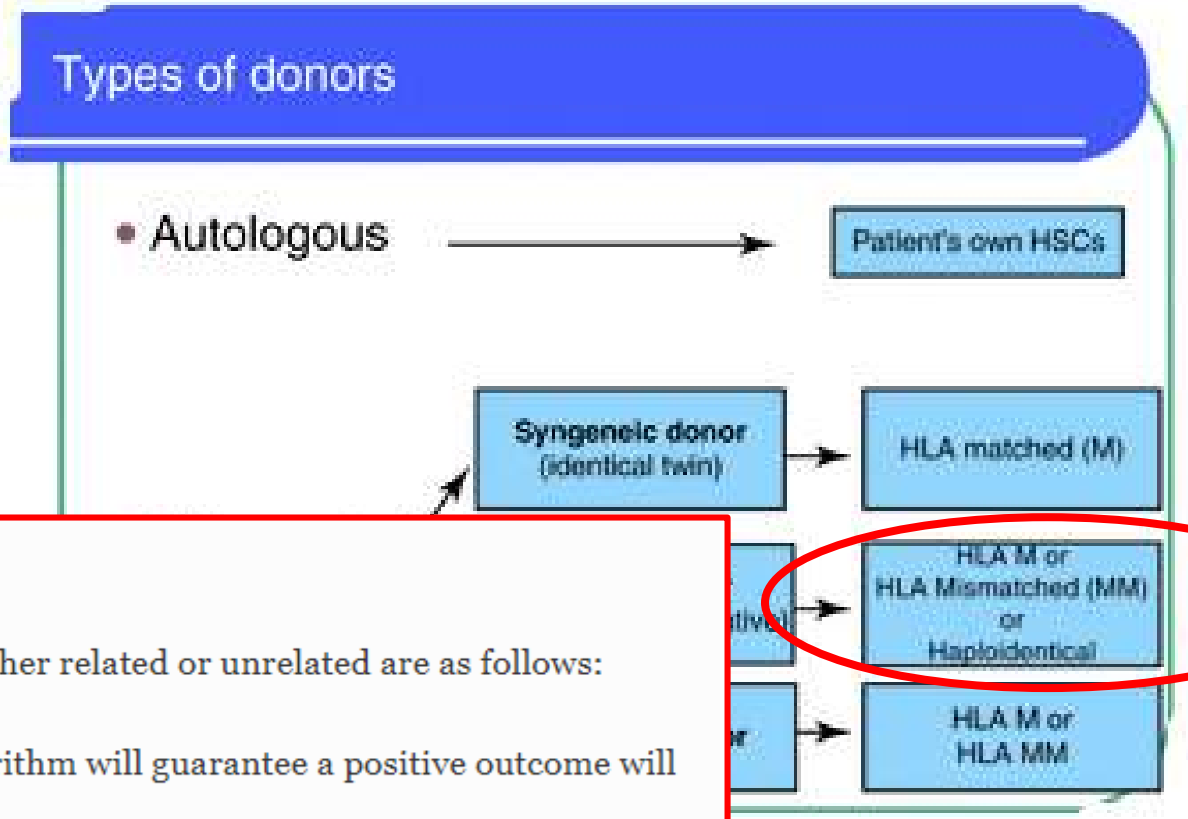
- Donor: Mother haploidentical
  HLA: 9/10
  HLA-A: 1 diferencie



STANDAR FOR HLA STUDY:
B2.11 Clinical Programs performing allogeneic transplantation shall use HLA testing laboratories that are capable of carrying out DNA–based intermediate and high resolution HLA-typing and are appropriately accredited by the American Society for Histocompatibility and Immunogenetics (ASHI), European Federation for Immunogenetics (EFI), or other accrediting organizations providing histocompatibility services appropriate for hematopoietic cellular therapy transplant patients.

Background & Introduction

There are three conditions which have to be met for a donor to be considered suitable – the donor needs to be suitably matched, healthy and
willing to donate (Kisch 2015).



3.4.1 Donor Selection

The main determinants when selecting a donor whether related or unrelated are as follows:

The "perfect" donor does not exist – no current algorithm will guarantee a positive outcome will always occur.

Níchonghaile M. (2018)

Background & Introduction

Clinical case presentations

- Donor: Mother haploidentical
  HLA: 9/10
  HLA-A: 1 difere

Donor Consent and Clearance

All donors should be reviewed and consented prior to the recipient commencing conditioning chemotherapy. They should be medically cleared and understand the implications if they withdraw their consent or participation once the recipient's conditioning has commenced.

M. Níchonghaile

B5: POLICIES AND STANDARD C

B5.1 The Clinical Progra
Procedures addressi
required in B4. Thes
and shall address at

B5.1.1 Recipient evaluation, selection, and treatment.

B5.1.2 Donor and recipient confidentiality.

B5.1.3 Donor and recipient consent.

B5.1.4 Donor screening, testing, eligibility determination, selection, and management.

B5.1.5 Management of donors who require central venous access.

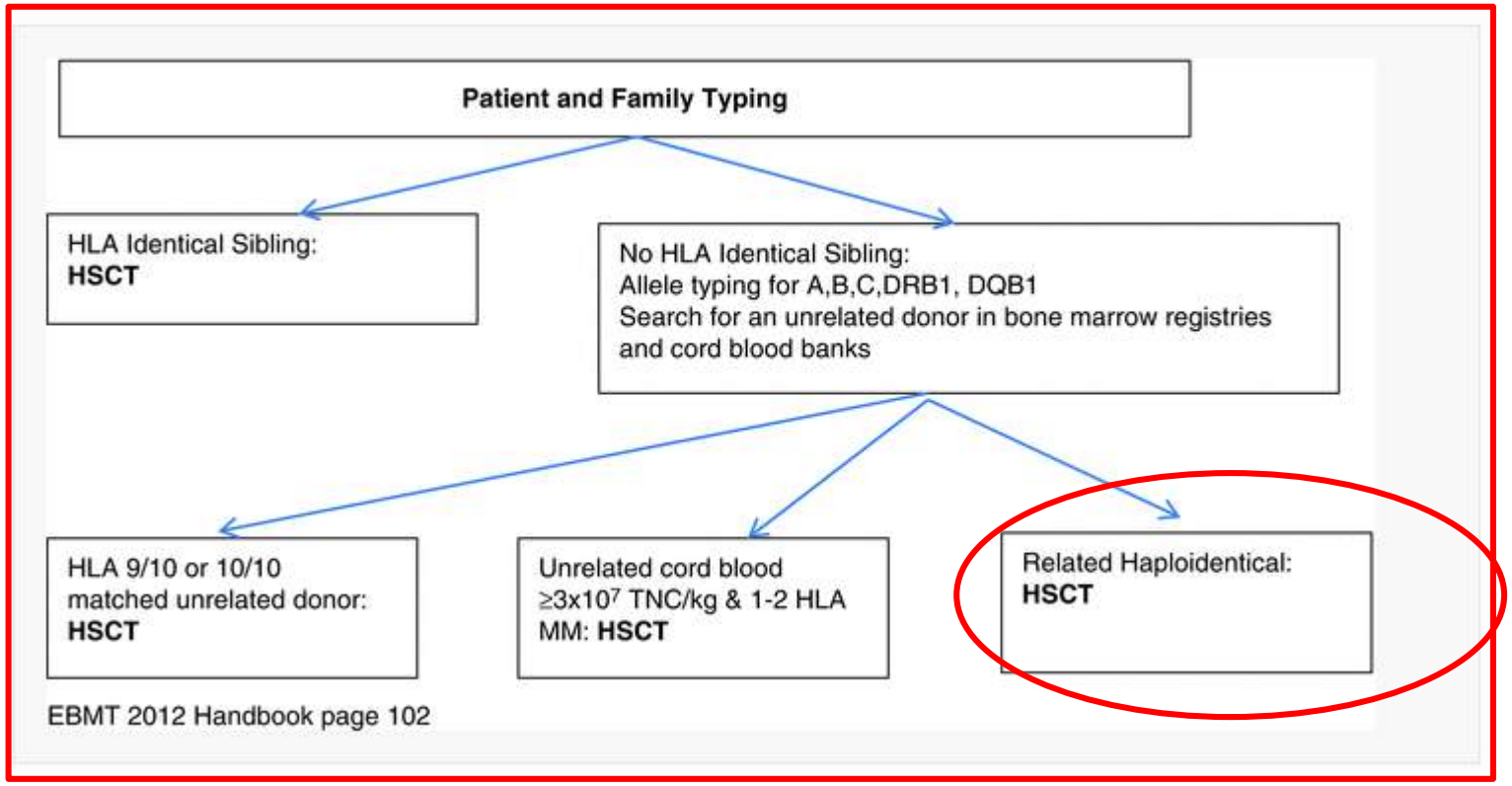
Table 3.4 Pre-transplant investigations of the donor

Blood group and antibody screening
Coagulation studies
Complete blood count
Full/confirmatory HLA typing
Liver function tests
ore antibody
Electrocardiogram
Under certain circumstances
Cytogenetic studies (chromosome fragility) if family history
Bone marrow examination
Echocardiogram or MUGA scan
Haemoglobin electrophoresis
Lung function tests
Haemoglobinopathy screen

Background & Introduction

Clinical case presentations

- Donor: Mother haploidentical
  HLA: 9/10
  HLA-A: 1 diferencie



Níchonghaile M. (2018)

Background & Introduction

Clinical case presentations

- **Diagnosis: Thalassemia major**
  - ❖ **CVC Hickman**
  - ❖ **Fertility preservation** (Biopsy)
- Supportive care : TPN
- Infection prophylaxis: Trimethoprim/ sulfamethoxazole
- Antifungal : Fluconazol
- Antiviral : Aciclovir

Background & Introduction

Clinical case presentations

- **Diagnosis: Thalassemia major**

❖ **CVC Hickman**

B3.7.4 There shall be written Standard Operating Procedures or guidelines for nursing procedures, including, but not limited to:

B3.7.4.6 Central venous access device care.

2. NEONATAL AND PEDIATRIC PATIENTS

Standard

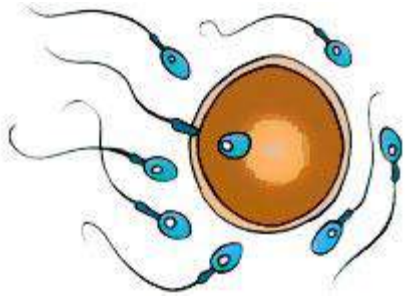
2.1 The nurse providing infusion therapy for neonatal and pediatric patients shall have clinical knowledge and technical expertise with respect to this population.
2.2 Clinical management of neonatal and pediatric patients shall be established in organizational policies, procedures, and/or practice guidelines and in accordance with applicable standards of practice.

Journal of Infusion Nursing
The Art and Science of Infusion Nursing

Background & Introduction

Clinical case presentations

- **Diagnosis: Thalassemia major**
- ❖**Fertility preservation** (Biopsy)



Bone Marrow Transplantation (2017), 1–10

ORIGINAL ARTICLE

Fertility preservation issues in pediatric hematopoietic stem cell transplantation: practical approaches from the consensus of the Pediatric Diseases Working Party of the EBMT and the International BFM Study Group

A Balduzzi1

JOURNAL OF CLINICAL ONCOLOGY | ASCO SPECIAL ARTICLE

Fertility Preservation for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update

Alison W. Loren, Pamela B. Mangu, Lindsay Nohr Beck, Lawrence Brennan, Anthony J. Magdalinski, Ann H. Partridge, Gwendolyn Quinn, W. Hamish Wallace, and Kutluk Oktay

Background & Introduction

Clinical case presentations

- **Diagnosis: Thalassemia major**
- **Conditioning regimen:**
- Tiotepa (-7)
- Fludarabine (-6,-5,-4,-3)
- Treosulphan (-6-5-4)

- **GvHD Prophilaxys:**
- Anti –thymocyte globulin (ATG)(-5,-4,-3)
- Cyclosporine (……-1)
- Methotrexate (+1, +3,+6)

Background & Introduction

Clinical case presentations

- **Diagnosis: Thalassemia major**
- **Conditioning regimen:**
- Tiotepa (-7)
- Fludarabine (-6,-5,-4,-3)
- Treosulphan (-6-5-4)

B3.7.3 Nurses shall have received specific training and maintain competence in the transplant-related skills that they routinely practice including:

B3.7.3.1 Hematology/oncology patient care, including an overview of the cellular therapy process.

B3.7.3.2 Administration of preparative regimens.

B3.7.3.3 Administration of blood products, growth factors, cellular therapy products, and other supportive therapies.

Background & Introduction

Clinical case presentations

- **Diagnosis: Thalassemia major**
- **Conditioning regimen:**
- Tiotepa (-7)
- Fludarabine (-6,-5,-4,-3)
- Treosulphan (-6-5-4)

- **Conditioning regimens** vary in doses and schedules based on the patient's disease, the type of transplant, and the goal of therapy (Harris, 2010).

- High-dose chemotherapy **preparative regimens** are combinations of the most effective agents for a particular disease that are given at high doses with the goal of total myeloablation (Childs, 2011; Polovich, Whitford, & Olsen, 2009)

Background & Introduction

Clinical case presentations

- **Diagnosis: Thalassemia major**
- **GvHD Prophilaxys:**
- Anti –thymocyte globulin (ATG)(-5,-4,-3)
- Cyclosporine (……-1)
- Methotrexate (+1, +3,+6)

Evidenced based practice & Indications

- B2.1 There shall be a designated inpatient unit of appropriate location and adequate space and design that minimizes airborne microbial contamination.
  B2.4 Facilities used by the Clinical Program shall be maintained in a clean, sanitary, and orderly manner.

- Isolation: Individual room
- HEPA filters with possitive pressure is recommended for high risk patients
- Infection control policies: Visits
- Auditing of airborne microbial infections in non-HEPA rooms should be performed
- SOP(s) on infection control, biosafety, and chemical and radiological safety should indicate how allocation of rooms is prioritized

Evidenced based practice & Indications

Clinical case presentations

- Diagnosis: Thalassemia major
- Transfusions needed
- Low bacterial diet
- Mucositis
- Nauseas and Vomiting
- Pain : assessement and control
- Psychological support
- Homecare after discharge

Evidenced based practice & Indications

Clinical case presentations :

B3.9 CONSULTING SPECIALISTS

B3.9.1 The Clinical Program shall have access to certified or trained consulting specialists and/or specialist groups from key disciplines who are capable of assisting in the management of recipients and donors requiring medical care, including, but not limited to:

B3.9.1.1 Surgery.

B3.9.1.2 Pulmonary medicine.

B3.9.1.3 Intensive care.

B3.9.1.4 Gastroenterology.

B3.9.1.5 Nephrology.

B3.9.1.6 Infectious disease.

B3.9.1.7 Cardiology.

B3.9.1.8 Pathology.

Conclusion

B3.6 CLINICAL TRANSPLANT TEAM

B3.6.1 Clinical Programs performing pediatric transplantation shall have a transplant team trained in the management of pediatric recipients.

B3.7.2 Clinical Programs treating pediatric recipients shall have nurses formally trained and experienced in the management of pediatric patients receiving cellular therapy.

Literature reference

1. Borte S[1], von Döbeln U, Hammarström L. **Guidelines for newborn screening of primary immunodeficiency diseases.** Curr Opin Hematol. 2013 Jan;20(1):48-54. doi: 10.1097/MOH.0b013e32835a9130.

2.- Alonso L[1], and al. **Haematopoietic stem cell transplantation in paediatric patients with β-thalassaemia and sickle cell disease: An experience of the Spanish Working Group for Bone Marrow Transplantation in Children (GETMON).** Med Clin (Barc). 2018 Jul 9. pii: S0025-7753(18)30333-6. doi: 10.1016/j.medcli.2018.05.013. [Epub ahead of print]

3.-Hladun R[1], Elorza I, Olivé T, Dapena JL, Llort A, Sánchez de Toledo J, Díaz de Heredia C.**Results of hematopoietic stem cell transplantation in hemoglobinopathies: thalassemia majorand sickle cell disease].** An Pediatr (Barc). 2013 Aug;79(2):75-82. doi: 10.1016/j.anpedi.2012.12.002. Epub 2013 Feb 9.

4.-Níchonghaile M. (2018) Donor Selection. In: Kenyon M., Babic A. (eds) **The European Blood and Marrow Transplantation Textbook for Nurses**. Springer, Cham

5.-**Hematopoietic Stem Cell Transplantation .A Manual for Nursing Practice**. Susan A. Ezzone, MS, RN, CNP, AOCNP®. ONCOLOGY NURSING SOCIETY

6.-Adler A[1.] **Infectious complications of implantable ports and Hickman catheters in paediatric haematology-oncology patients.** J Hosp Infect. 2006 Mar;62(3):358-65. Epub 2006 Jan 10.

7.-**Fertility preservation issues in pediatric hematopoietic stem cell transplantation: practical approaches from the consensus of the Pediatric Diseases Working Party of the EBMT and the International BFM Study** . Group.A Balduzzi et al. Bone Marrow Transplantation (2017), 1–10

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EBMT
European Society
for Blood and Marrow Transplantation

Thank you

Quality Indicators for BMT-1st level FACT/JACIE accreditation

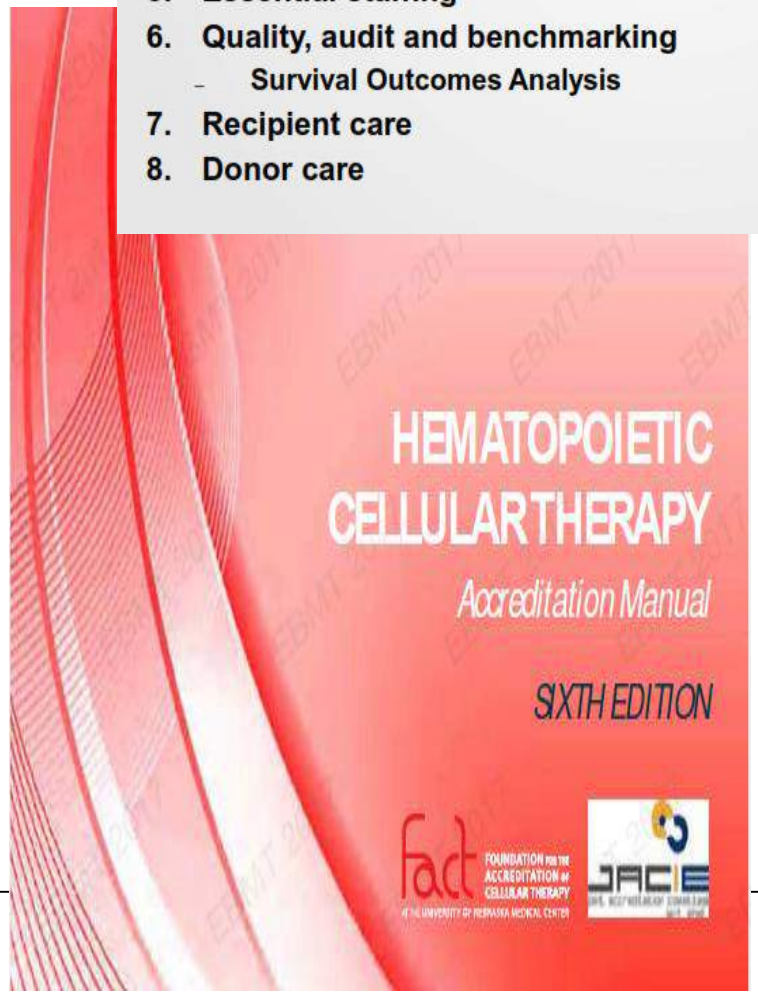
Aleksandra Babic, QM, JACIE QM Inspector
IOSI, Bellinzona, Switzerland

Nurses No Frontiers - Training course for HSCT nurses – India

14th -15th December 2018 , Khanolkar Auditorium, ACTREC, Tata Memorial Centre, Kharghar, Navi Mumbai

JACIE –overall umbrella

1. Clinical programme organisation
2. Ambulatory care
3. Accreditation for HLA and chimerism
4. Training, education & skills
5. Essential staffing
6. Quality, audit and benchmarking
   - Survival Outcomes Analysis
7. Recipient care
8. Donor care



B1 General	CM1 General	C1 General	D1 General
B2 Clinical Unit	CM2 Marrow Collection Facility	C2 Apheresis Facility	D2 Processing Facility
B3 Personnel	CM3 Personnel	C3 Personnel	D3 Personnel
B4 Quality Management	CM4 Quality Management	C4 Quality Management	D4 Quality Management
B5 Policies and Procedures	CM5 Policies and Procedures	C5 Policies and Procedures	D5 Policies and Procedures
B6 Allogeneic and Autologous Donor Selection, Evaluation, and Management	CM6 Allogeneic and Autologous Donor Evaluation and Management	C6 Allogeneic and Autologous Donor Evaluation and Management	D6 Process Controls
B7 Therapy Administration	CM7 Coding and Labeling of Cellular Therapy Products	C7 Coding and Labeling of Cellular Therapy Products	D7 Coding and Labeling of Cellular Therapy Products
B8 Clinical Research	CM8 Process Controls	C8 Process Controls	D8 Distribution
B9 Data Management	CM9 Cellular Therapy Product Storage	C9 Cellular Therapy Product Storage	D9 Storage
	CM10 Cellular Therapy Product Transportation and Shipping	C10 Cellular Therapy Product Transportation and Shipping	D10 Transportation, Shipping, and Receipt
			D11 Disposal
B10 Records	CM11 Records	C11 Records	D12 Records
	CM12 Direct Distribution to Clinical Program	C12 Direct Distribution to Clinical Program	

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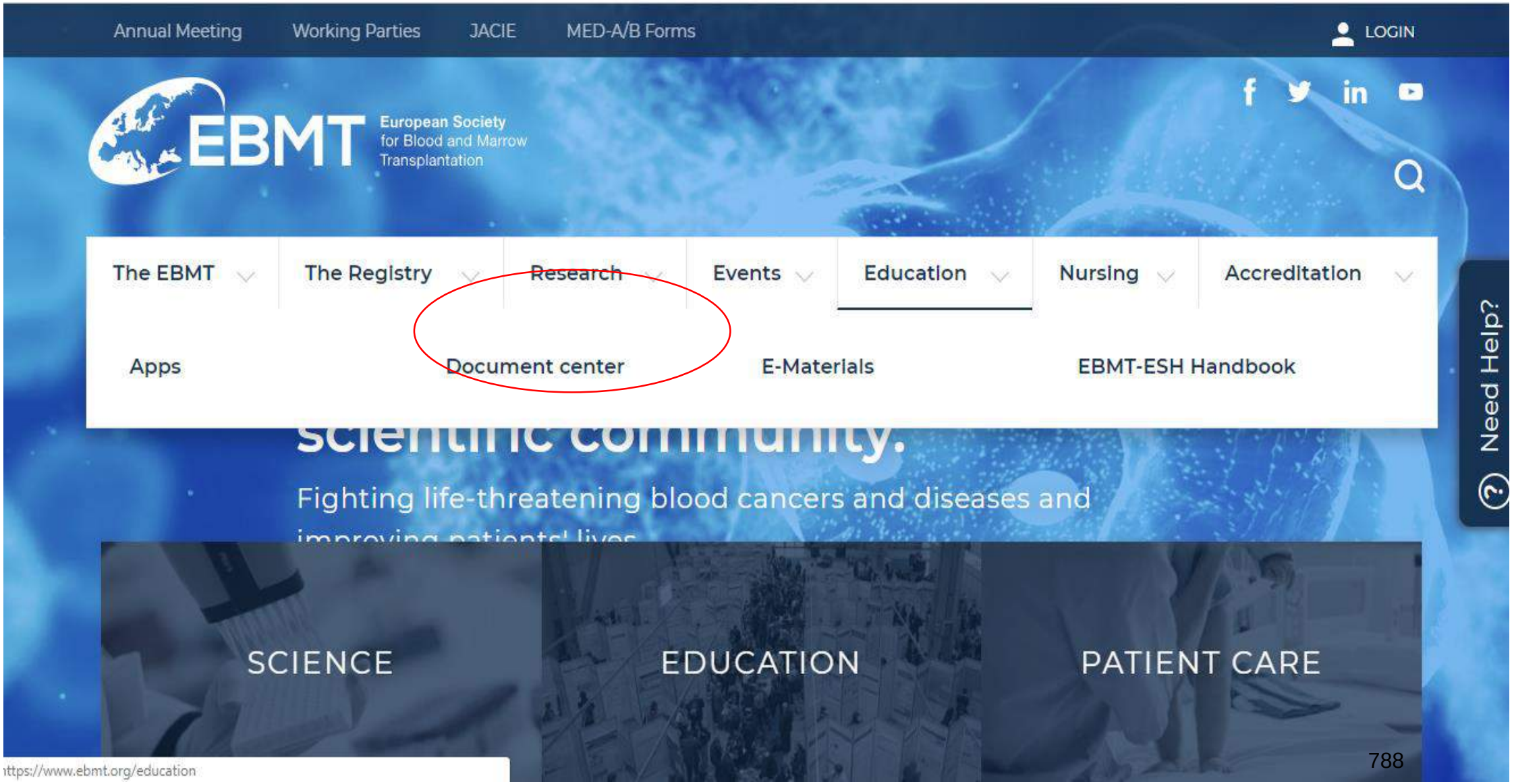

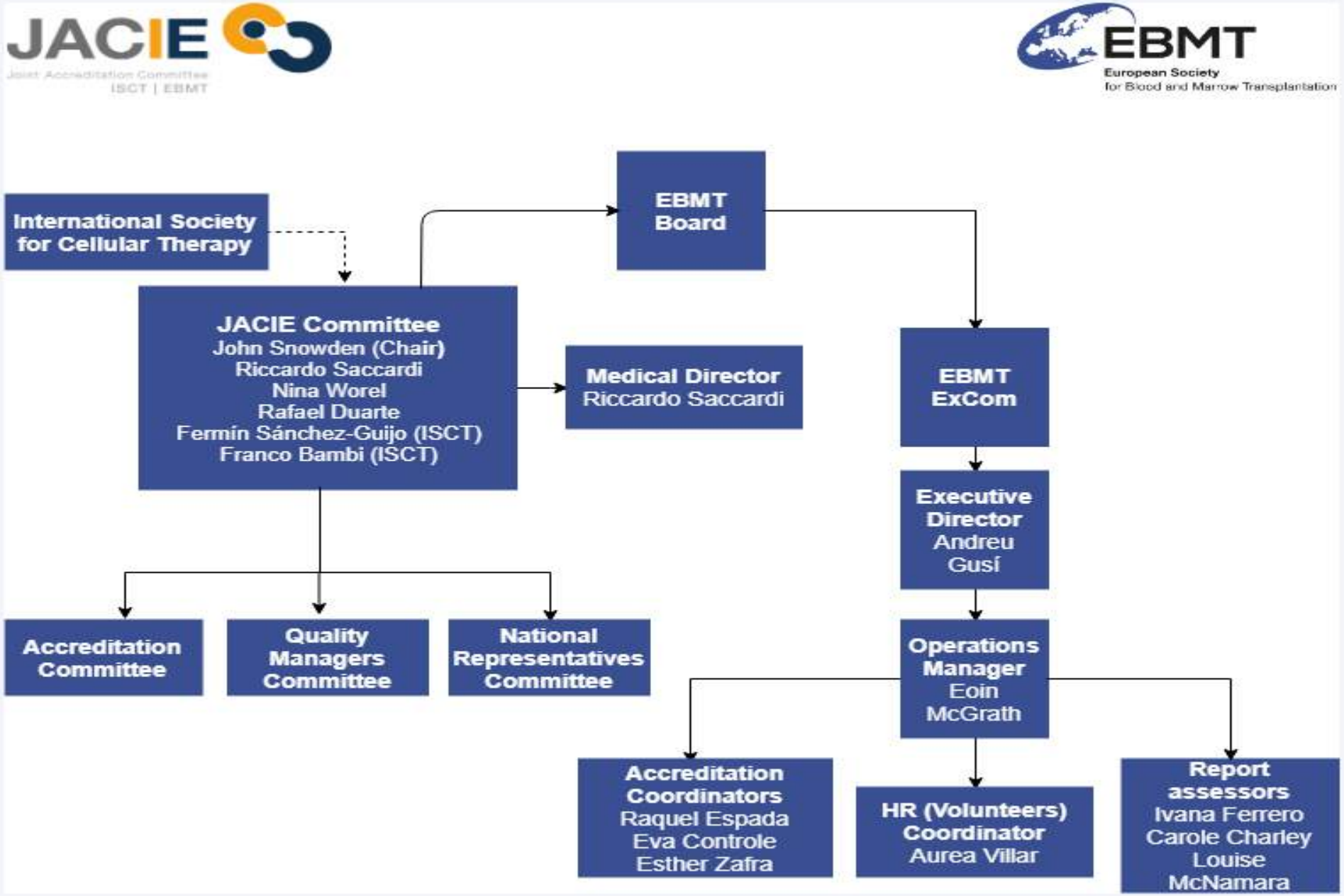
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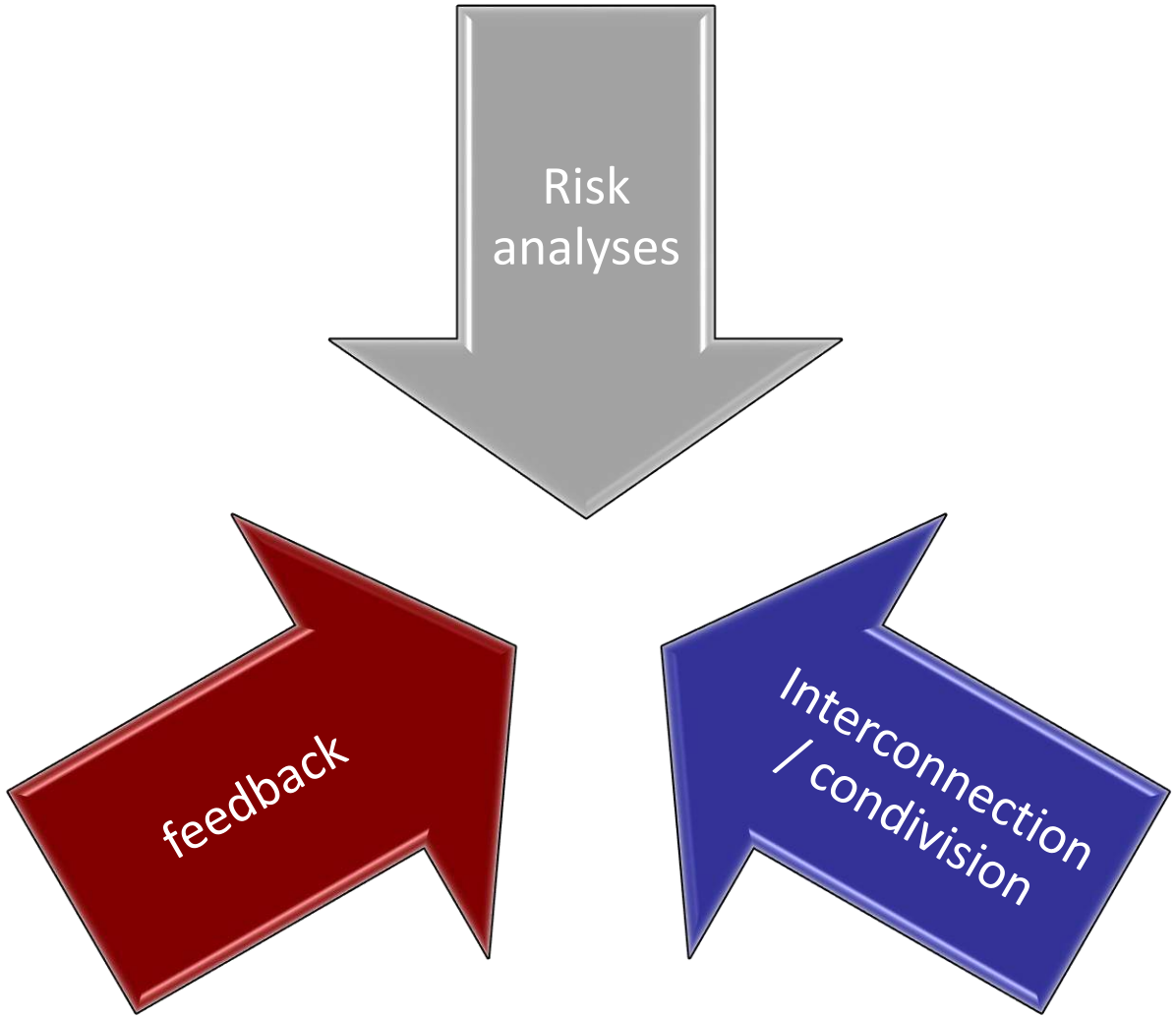
7° edition standards concepts



C2.4	There shall be a written assessment of critical Apheresis Collection Facility parameters that may affect cellular therapy product viability, integrity, contamination, or cross-contamination during collection.	Moderate
C2.4.1	The written assessment shall include temperature and humidity at a minimum.	Separated
C2.11	All waste generated by the Apheresis Collection Facility activities shall be disposed of in a manner that minimizes any hazard to facility personnel and to the environment in accordance with applicable laws and regulations.	New
C2.12	Gloves and protective clothing shall be worn while handling biological specimens. Such protective clothing shall not be worn outside the work area.	New

C3.1.1	There shall be an Apheresis Collection Facility Director with a medical degree or degree in a relevant science, with two (2) years of postgraduate training and experience in cellular therapy product collection procedures at a minimum. The Apheresis Collection Facility Director may also serve as the Apheresis Collection Facility Medical Director, if appropriately credentialed.	Significant
D3.2.3	The Processing Facility Medical Director shall have performed or supervised a minimum of five (5) cellular therapy product processing procedures in the twelve (12) month period preceding initial accreditation and a minimum average of five (5) cellular therapy product processing procedures per year within each accreditation cycle.	new
D3.2.4	The Processing Facility Medical Director shall participate in a minimum of ten (10) hours of educational activities related to cellular therapy annually.	Reordered

APPLICATION FOR FIRST-TIME ACCREDITATION & RE-ACCREDITATION

Instructions for completing the Application Form

Note: From 28/02/2011, centres applying for the first time must submit the completed **Inspection Checklist** before an application can be assessed and approved.
The Checklist can be downloaded from www.jacie.org/document-centre.
Applications for re-accreditation should submit the Inspection Checklist with the pre-inspection documentation **within 30 days** of the application approval date.

1. GENERAL DETAILS

Programme name[1]: Unità Trapianti dell'Istituto Oncologico della Svizzera Italiana
Country: Ospedale Regionale di Bellinzona e Valli, CH-6500 Bellinzona, Switzerland
Working language of centre: Italian

1.1. Contact details

There should be one designated person responsible for contact with the JACIE Office. Their details should be provided below. The applicant is responsible for ensuring that any changes to contact information are promptly communicated to the JACIE Office. Failure to do so may result in delays during the process.

Title: RN
First Name: Aleksandra
Family Name: Babic
Institution: Oncology Institute of Southern Switzerland (IOSI)
Address 1: Transplant Unit
Address 2: Ospedale Bellinzona e Valli , Bellinzona

Name of Document: R-001-03-Inspection Report Approved by: Eoin McGrath Responsible: Eoin McGrath Entry: Report the findings of an Inspection	Creation date: 17/06/2013 Effective date: 28/06/2013 Review date: 01/06/2014 Modification: Updated Instructions and included QM section	JACIE joint accreditation comittee isct-ebmt

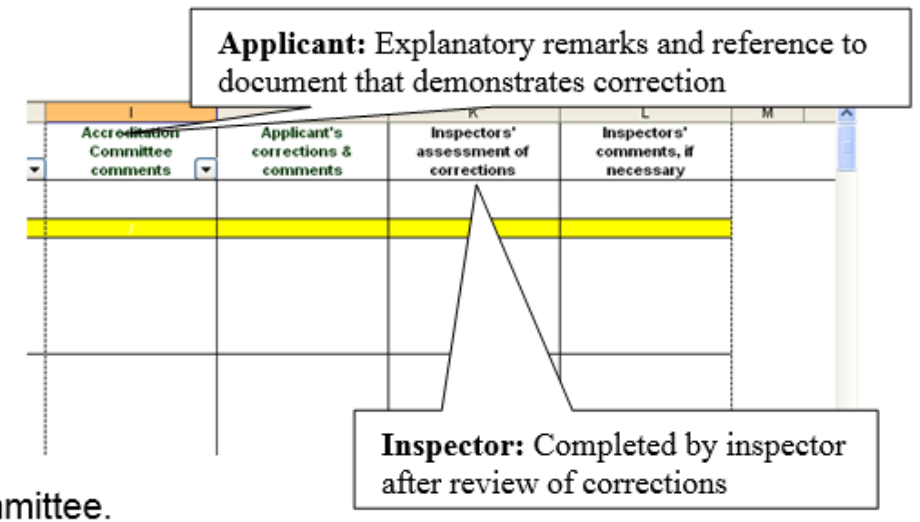
Inspection Summary Report

Inspection Report and Recommendations to Applicant

General Directions Given to Programmes for Correcting Cited Deficiencies:

Where issues have been identified, the following steps must be completed:

1. You must document in writing how your programme has corrected each of the deficiencies. Correction of deficiencies may take the form of a new protocol or procedure, a revised protocol or procedure, new forms developed and put into use, new staff, new training processes, etc.
   Enter this information into the corresponding section of the *Inspection Checklist* aligning the corrections information with the remarks of the inspector and/or the Accreditation Committee.



2. **Labels**: corrections to labels should be detailed in a separate document. This could be a simple Word document. Entitle this document as “Labelling response and corrections” and refer to the type of label which has been corrected or amended. For example, “C7.5.1 Apheresis label at completion of collection”.

Inspector: All items compliant?
No

Step Number	Ref.	Estándares	Applicant's Self-assessment	Source of evidence and explanatory text	Inspector's Assessment	Inspector's Comments *(support your answers with additional informatio*	Accreditation Committee comments	Applicant's corrections & comments - 1	Inspectors' assessment of corrections -1	Inspectors' comments, if necessary -1	Applicant's corrections & comments -2	Inspectors' assessment of corrections - 2	Inspectors' comments, if necessary - 2
1	B1.2	Los Programas Clínicos deben utilizar instituciones de recolección y procesamiento que cumplan con		Submit evidence									
1	B1.3	El Programa Clínico debe cumplir con las leyes y regulaciones correspondientes.											
				Submit evidence									
1	B1.3.1	El Programa Clínico debe contar con licencia, estar registrado, o acreditado por las autoridades											
				Submit evidence									
2	B1.4	El Programa Clínico debe contar con un equipo de trasplante designado que incluya al Director del Programa Clínico, un Manager de Calidad y al menos un (1) Médico de trasplante adscrito		Submit evidence									
2	B1.5	El Programa Clínico debe cumplir con la tabla Número Mínimo de Pacientes de Nuevo Ingreso para Acreditación que se encuentra en el Apéndice I.		*Indicate total number of transplants of each type performed in last 12 months*		*Indicate total number of transplants of each type performed in last 12 months*							

Part D: Cell Processing

Inspector: All items compliant? No

Step Number	Ref.	Standard	Estándares	Applicant's Self-assessment	Source of evidence and explanatory text	Inspector's Assessment	Inspector's Comments *(support your answers with additional information)*	Accreditation Committee comments	Appl
	D1	GENERAL	GENERAL						
1	D1.1	These Standards apply to all processing, storage, and distribution activities performed in the Processing Facility on cellular therapy products obtained from living donors.	Estos estándares aplican a todas las actividades de procesamiento, almacenamiento y distribución llevadas a cabo en la Institución de Procesamiento para todos aquellos productos de terapia celular que son obtenidos a partir de donantes vivos.						
1	D1.2	The Processing Facility shall abide by all applicable laws and regulations.	La Institución de Procesamiento debe cumplir con todas las leyes y regulaciones aplicables.		Submit evidence				
1	D1.2.1	The Processing Facility shall be licensed, registered, or accredited as required by the appropriate governmental authorities for the activities performed.	La Institución de Procesamiento debe estar registrada, aprobada, y/o acreditada por las autoridades gubernamentales correspondientes en cuanto a las funciones que realiza.						
2	D1.3	The Processing Facility shall have a Processing Facility Director, a Processing Facility Medical Director and Quality Manager, at least one designated staff member actively performing cellular therapy product processing. This team shall have been in place for at least twelve (12) months preceding initial accreditation.	La Institución de Procesamiento debe contar con un Director de la Institución, un Director Médico de la Institución, un Manager de Calidad y al menos un miembro designado del personal, y que lleve a cabo de forma activa procesamiento de productos de terapia celular. Este equipo debe haber iniciado funciones por al menos doce (12) meses previos a la						
	D2	PROCESSING FACILITY	INSTITUCIÓN DE PROCESAMIENTO						
1	D2.1	The Processing Facility shall be of adequate space, design, and location, for the intended procedures.	La Institución de Procesamiento debe ser de un tamaño adecuado, diseño y ubicación para los procedimientos que se realizan.		Submit evidence				
1	D2.1.1	The Processing Facility shall provide adequate lighting, ventilation, and access to sinks to prevent the introduction, transmission, or spread of communicable disease.	La Institución de Procesamiento debe proveer adecuada iluminación, ventilación, tener acceso a lavabos o tarjas, con el fin de prevenir la introducción, transmisión y diseminación de enfermedades infecciosas		Submit evidence				

Part D: Quality Management

Inspector: All items compliant?
No

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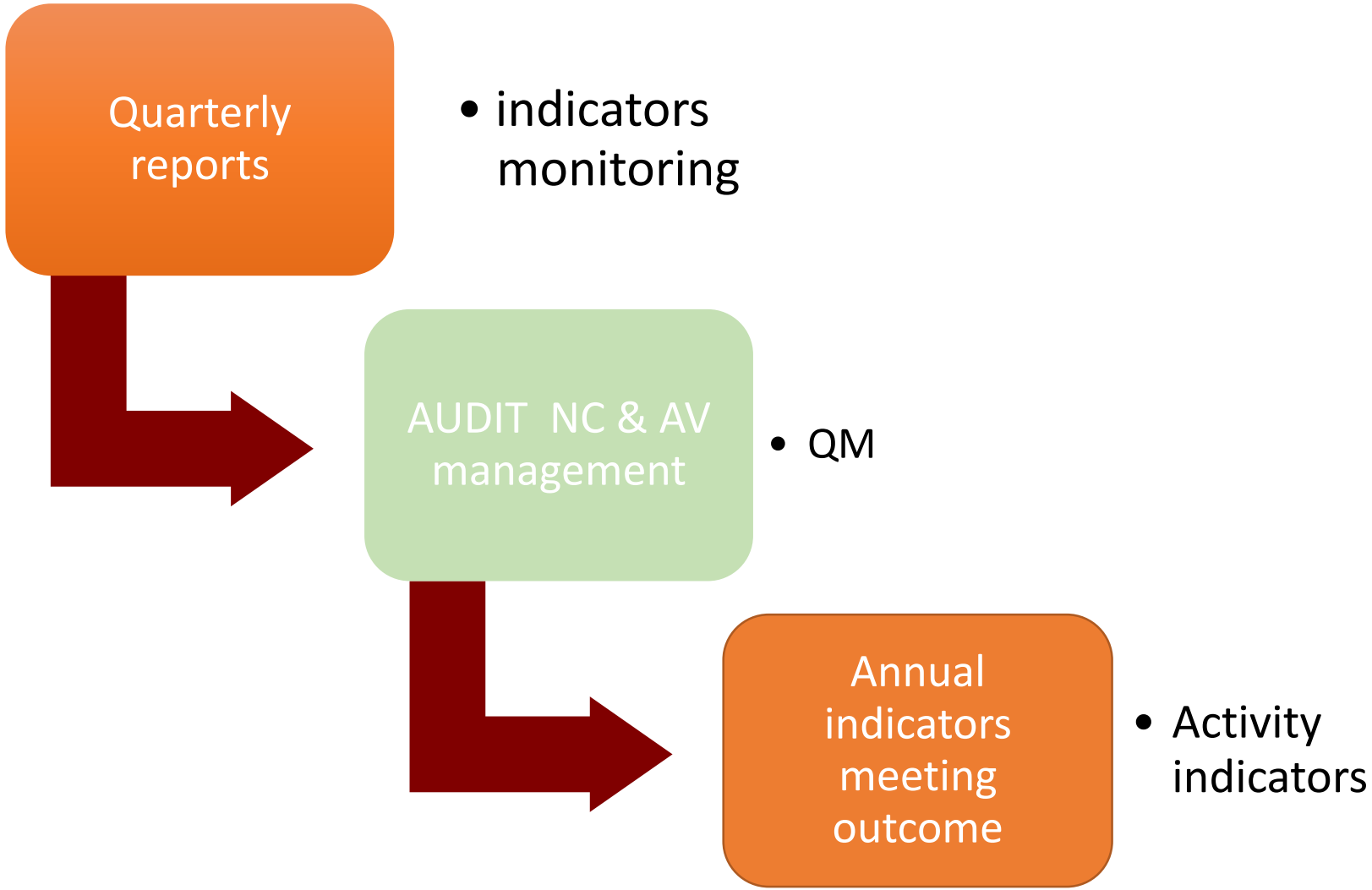
Ref.	Standard	Applicant's assessment	Source of evidence and explanatory text	Inspector's Assessment	Inspector's Comments *(support your answers with additional information)*	Accreditation Committee comments	Applicant's corrections & comments - 1	Inspectors' assessment of corrections	Inspectors' comments, if necessary -1	Applicant's corrections & comments -2	Inspectors assessme of correcti 2
D.04.05.03.08	A system for record creation, assembly, review, storage, archival, and retrieval.	Compliant	~~POS.T.750.01~~ Gestione documenti e registrazioni	Compliant							
D.04.06	The Quality Management Plan shall include, or summarize and reference, policies and procedures for establishment and maintenance of written agreements with third parties whose services impact the cellular therapy product.	Compliant		Compliant							
D.04.06.01	Agreements shall include the responsibility of the facility performing any step in processing, testing, or storage to comply with applicable laws and regulations and these Standards.	Compliant		Partially compliant	agreements are generic and not detailed						
D.04.06.02	Agreements shall be dated and reviewed on a regular basis.	Compliant		Non-compliant	dates are not stated						
D.04.08	The Quality Management Plan shall include, or summarize and reference, policies, procedures, and a schedule for conducting, reviewing, and reporting audits of the Processing Facility's activities to verify compliance with elements of the Quality Management Program and operational policies and	Compliant	~~POS.T.920.01~~ AUDIT INTERNI	Partially compliant	There is no prospective calendar of audits, there is no evidence of interaction between different QMs						
D.04.08.01	Audits shall be conducted on a regular basis by an individual with sufficient expertise to identify problems, but who is not solely responsible for the process being audited.	Compliant	~~POS.T.920.01~~ AUDIT INTERNI	Partially compliant	excel sheet						
D.04.08.02	The results of audits shall be used to recognize problems, detect trends, identify improvement opportunities, implement corrective and preventive actions when necessary, and follow-up on the effectiveness of these actions in a timely manner.	Compliant	~~POS.T.920.01~~ AUDIT INTERNI	Partially compliant	not enough evidence on treacable process and closing NC						
D.04.08.03	Documentation that external facilities performing critical contracted services have met the requirements of the written agreements shall be audited annually.	Compliant	~~POS.T.920.01~~ AUDIT INTERNI	Partially compliant	SIMT expired, some copies available, not treacable						
D.04.09	The Quality Management Plan shall include, or summarize and reference, policies and procedures on the management of cellular therapy products with positive microbial culture results that address at a minimum:	BLANK CELL	~~BLANK CELL~~	BLANK CELL	BLANK CELL	BLANK CELL	BLANK CELL	BLANK CELL	BLANK CELL	BLANK CELL	BLANK CI
D.04.09.01	Documentation and product labeling.	Compliant	~~POS.T.852.01~~ ETICHETTATURA PRODOTTI CELLULARI	Non-compliant	missing the list of labels						

06.1 ref	6.1 standard	07ref	07 standard	Changes 6.01-7
C04.14.02.06	Review and approval of the validation plan, results, and conclusion by the Apheresis Collection Facility Director or designee and the Quality Manager or designee.	C4.14.2.7	Review and approval of the validation plan, validation report, and conclusion by the Quality Manager or designee and the Apheresis Collection Facility Director or designee.	Negligible
C04.14.03	Changes to a process shall include evaluation of risk to confirm that they do not create an adverse impact anywhere in the operation and shall be validated or verified as appropriate.	C4.14.3	Significant changes to critical procedures shall be validated and verified as appropriate.	Moderate
		C4.15	The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the evaluation of risk in changes to a process to confirm that the changes do not create an adverse impact or inherent risk elsewhere in the operation.	New
		C4.16	The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for obtaining feedback.	New
		C4.16.1	Feedback shall be obtained from associated Clinical Programs and Processing Facilities.	New
		C4.16.2	Feedback shall be obtained from donors or legally authorized representatives.	New
		C4.17.1	Meetings should have defined attendees, documented minutes, and assigned actions.	New
		C4.17.2	Key performance data and review findings shall be reported to staff.	New
		C4.18.1	The annual report and documentation of the review findings shall be made available to key personnel, the Clinical Program Director, and the Processing Facility Director.	New
C05	**POLICIES AND PROCEDURES**	**C5**	**POLICIES AND STANDARD OPERATING PROCEDURES**	Negligible

07ref	07 standard	Changes 6.01-7
D4.15	The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for the evaluation of risk in changes to a process to confirm that the changes do not create an adverse impact or inherent risk elsewhere in the operation.	New
D4.16	The Quality Management Plan shall include, or summarize and reference, policies and Standard Operating Procedures for obtaining feedback.	New
D4.16.1	Feedback shall be obtained from associated Clinical Programs and Collection Facilities.	New
D4.17	The Processing Facility Director or designee shall review the Quality Management activities with representatives in key positions in all elements of the cellular therapy program, at a minimum, quarterly.	New
D4.17.1	Meetings should have defined attendees, documented minutes, and assigned actions.	New
D4.17.2	Key performance data and review findings shall be reported to staff.	New
D4.18.1	The annual report and documentation of the review findings shall be made available to key personnel, the Clinical Program Director, and the Collection Facility Director.	New

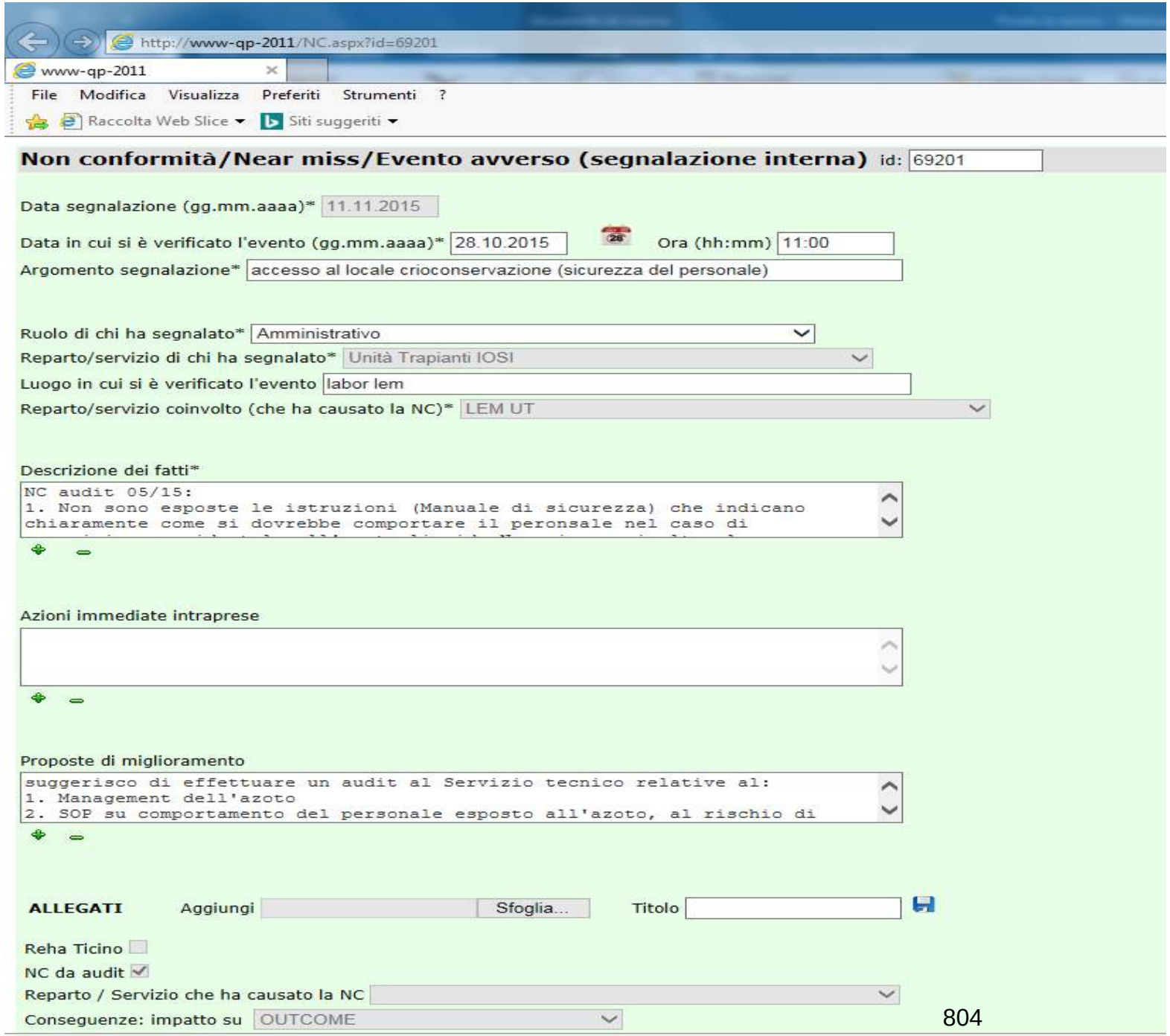
Feedback = documents sharing &meetings



1. Audits
2. REPORTING

Non conformity
Near miss
Adverse events

3.ANALYSES
4. MEETINGS WITH DEDICATED TEAM
5. IMPROVEMENT



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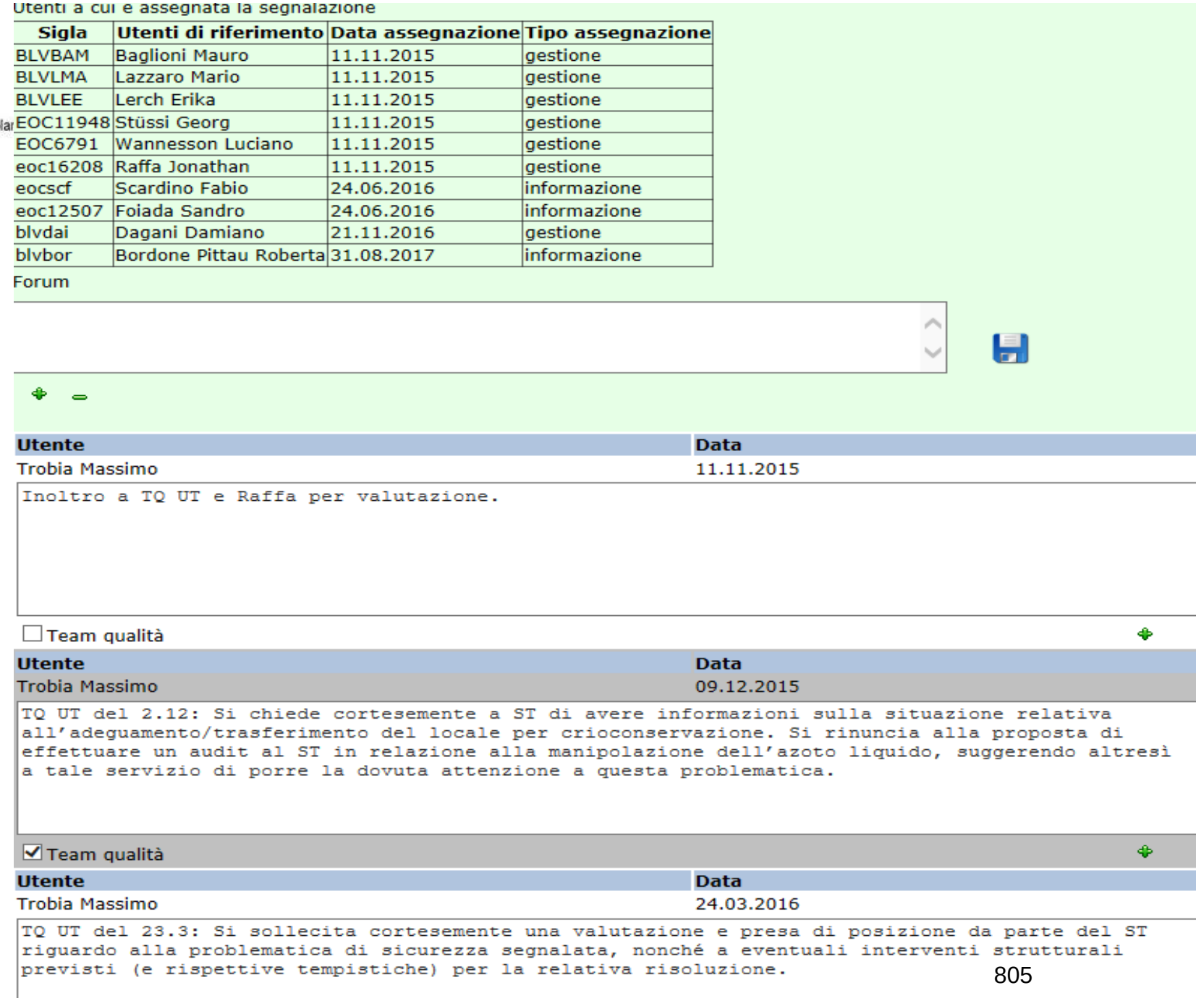

Utenti a cui è assegnata la segnalazione

Sigla	Utenti di riferimento	Data assegnazione	Tipo assegnazione
BLVBAM	Baglioni Mauro	11.11.2015	gestione
BLVLMA	Lazzaro Mario	11.11.2015	gestione
BLVLEE	Lerch Erika	11.11.2015	gestione
EOC11948	Stüssi Georg	11.11.2015	gestione
EOC6791	Wannesson Luciano	11.11.2015	gestione
eoc16208	Raffa Jonathan	11.11.2015	gestione
eocscf	Scardino Fabio	24.06.2016	informazione
eoc12507	Foiada Sandro	24.06.2016	informazione
blvdai	Dagani Damiano	21.11.2016	gestione
blvbor	Bordone Pittau Roberta	31.08.2017	informazione

Forum

Utente	Data
Trobia Massimo	11.11.2015

Inoltro a TQ UT e Raffa per valutazione.

☐ Team qualità

Utente	Data
Trobia Massimo	09.12.2015

TQ UT del 2.12: Si chiede cortesemente a ST di avere informazioni sulla situazione relativa all'adeguamento/trasferimento del locale per crioconservazione. Si rinuncia alla proposta di effettuare un audit al ST in relazione alla manipolazione dell'azoto liquido, suggerendo altresì a tale servizio di porre la dovuta attenzione a questa problematica.

☑ Team qualità

Utente	Data
Trobia Massimo	24.03.2016

TQ UT del 23.3: Si sollecita cortesemente una valutazione e presa di posizione da parte del ST riguardo alla problematica di sicurezza segnalata, nonché a eventuali interventi strutturali previsti (e rispettive tempistiche) per la relativa risoluzione.

1. Audits
2. REPORTING

Non conformity
Near miss
Adverse events

3.ANALYSES
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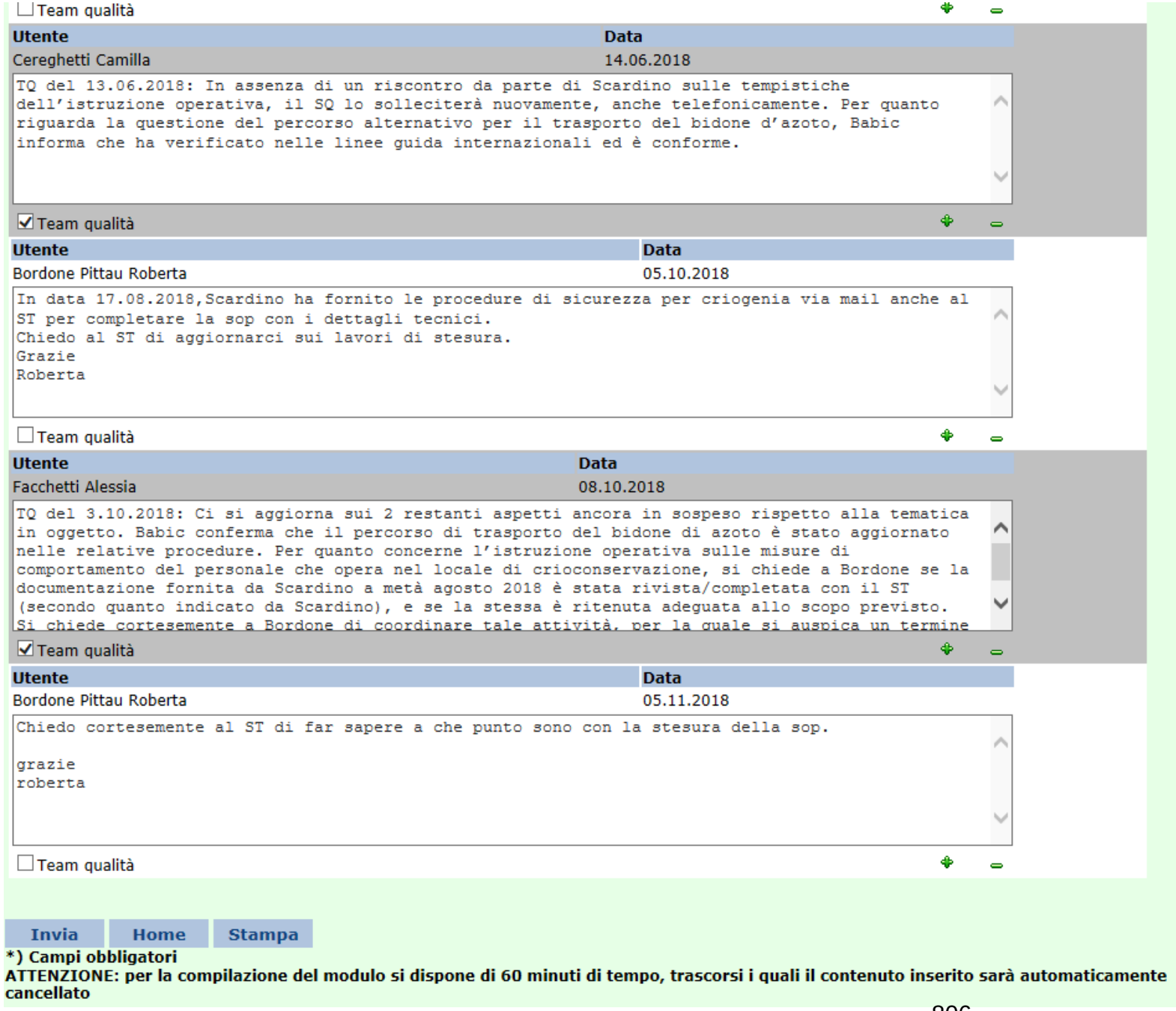

Team qualità

Utente	Data
Cereghetti Camilla	14.06.2018

TQ del 13.06.2018: In assenza di un riscontro da parte di Scardino sulle tempistiche dell'istruzione operativa, il SQ lo solleciterà nuovamente, anche telefonicamente. Per quanto riguarda la questione del percorso alternativo per il trasporto del bidone d'azoto, Babic informa che ha verificato nelle linee guida internazionali ed è conforme.

☑ Team qualità

Utente	Data
Bordone Pittau Roberta	05.10.2018

In data 17.08.2018,Scardino ha fornito le procedure di sicurezza per criogenia via mail anche al ST per completare la sop con i dettagli tecnici.
Chiedo al ST di aggiornarci sui lavori di stesura.
Grazie
Roberta

☐ Team qualità

Utente	Data
Facchetti Alessia	08.10.2018

TQ del 3.10.2018: Ci si aggiorna sui 2 restanti aspetti ancora in sospeso rispetto alla tematica in oggetto. Babic conferma che il percorso di trasporto del bidone di azoto è stato aggiornato nelle relative procedure. Per quanto concerne l'istruzione operativa sulle misure di comportamento del personale che opera nel locale di crioconservazione, si chiede a Bordone se la documentazione fornita da Scardino a metà agosto 2018 è stata rivista/completata con il ST (secondo quanto indicato da Scardino), e se la stessa è ritenuta adeguata allo scopo previsto. Si chiede cortesemente a Bordone di coordinare tale attività, per la quale si auspica un termine

☑ Team qualità

Utente	Data
Bordone Pittau Roberta	05.11.2018

Chiedo cortesemente al ST di far sapere a che punto sono con la stesura della sop.

grazie
roberta

☐ Team qualità

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*) Campi obbligatori
ATTENZIONE: per la compilazione del modulo si dispone di 60 minuti di tempo, trascorsi i quali il contenuto inserito sarà automaticamente cancellato

Protocollo finale prodotto di leucaferesi

Data di raccolta	01.10.2018	02.10.2018
Numero LAF	18/14A	18/14B
Numero analisi		
Peso	90.0	90.0
Biohazard	nessuno	nessuno
CD34 % SP pre %	0.08	0.21
CD34 SP pre (/µl)	23	69
CD34 % LAF %	0.55	1.26
CD34 LAF: (x 10^6/kg)	2.93	7.40
Volume sacca congelata (ml)	60	60
N° sacche congelate:	2	2
CD 34 / sacca (x10`6/kg)	1.47	3.70
Vitalità pre-congelo (%)	99	99
Resa aferetica	79	75
CD34 x 10^6/Kg disp. post manip.	2.90	6.84
Leuco/sacca post-manip.(x10^9/l)	251.6	300.2
Colture batteriologia	Negativa	Negativa
Lavorazione eseguita da	Eugenia Schipani	Micaela Pellegrini
Lavorazione eseguita il	02.10.2018 10:00	03.10.2018 10:00
Congelamento eseguito il	02.10.2018 11:15	03.10.2018 11:10

In data 2 e 3 ottobre 2018 sono state crioconservate 4 sacche per un totale di CD34+ pari a 930.14 X 10^6 (10.33 X 10^6/kg).

BIOHAZARD: Nessuno

Il materiale crioconservato é idoneo e sufficiente per due trapianti di cellule staminali periferiche.

Annual report: Indicators

Collection

- % efficiency
- % positive cultural products
- Adverse events
- Algorythms analyses
- Collection target achievement
- Purity index

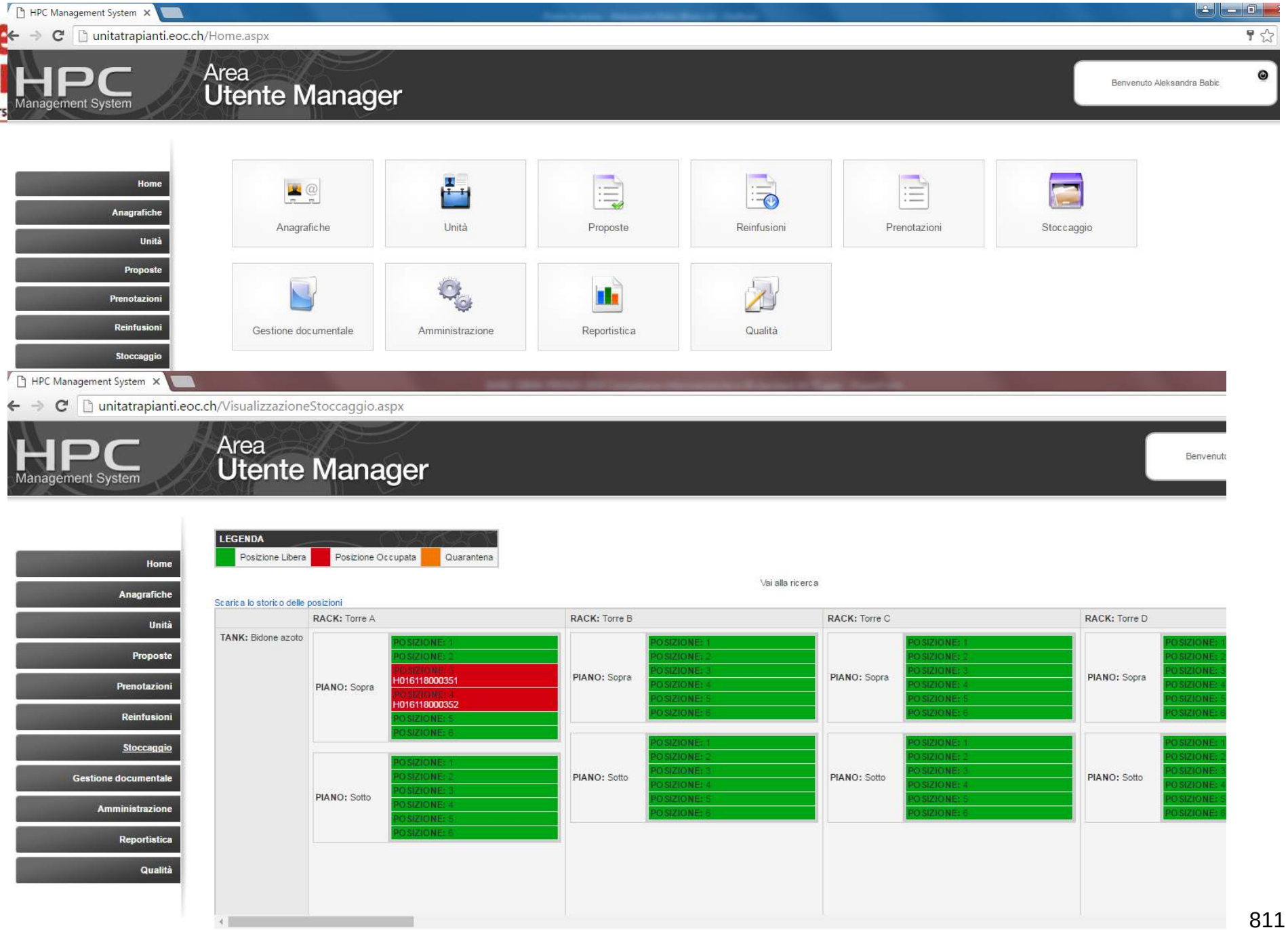
Processing

- vitality
- Stem cells recovery
- Product sterility
- Engraftment
- SC Dose releised

Summary of indicators

	Target	Risultato
Pts entered the transplant program	< 20%	13.7
2 y overall survival (Mieloma – Linfoma)	≥ 70%	76%
Pts died by D100 (pts selection capacity)	< 5%	0
Time of hospitalization from D0	< 21	22.7
Pts recovered up to D100	< 20%	4.1
LAF during WE or festivity	< 5%	2.3
Apheresis efficiency	> 50%	59
N° LAF per transplant	< 2	2
N° bags HSC with bact. +	0	1
ANC median engraftment time	≤ 14	10
PLT median engraftment time	≤ 20	14
N° bags with cryopreservaton difficulties	0	0
CD34 vitality before cryio	≥ 80%	96
CD34 vitality post elaboration	≥ 80%	96
CD34 recovery post elaboration	≥ 68%	90
Post lavoration ANC recovery	≥ 55%	89

	D	E	F	G	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ	AR	AS
4	N° progress	Data di nascita	Sesso M=1 F=2	Data diagnos	ECOG PS good= 0-1 poor= 2-4	CT condizionamento	D1 condizion.	Data trapianto	tipo di cellule trapiantate ABMT=1 PBSCT=2 ABMT+PBSCT=3	N° cell reinfuse x10^7	N°CD34+ reinfusi x10*6/Kg	1° giorno con ANC > 500	1° giorno pl > 50 G/l spontanee	1° giorno pl > 20 G/l spontanee	giorno di ricovero trapianto	dimissione dopo trapianto	Stato di malattia al postrapianto PR=1; CR=2; PD=3 stable disease(NC)=4 n.a.=5
23		23.09.1973	1	14.10.20	0	6	05.05.2016	11.05.2016	2	.	6.36	22.05.2016	.	25.05.2016	04.05.2016	02.06.2016	2
24		04.11.1955	1	05.10.20	0	15	26.05.2016	27.05.2016	2	.	3.96	08.06.2016	.	11.06.2016	25.05.2016	13.06.2016	2
25		24.09.1956	1	19.04.20	0	6	02.06.2016	08.06.2016	2	.	3.19	20.06.2016	.	22.06.2016	01.06.2016	25.06.2016	2
26		08.04.1953	1	22.10.20	0	6	16.06.2016	22.06.2016	2	.	3.93	02.07.2016	.	03.07.2016	15.06.2016	06.07.2016	2
27		02.07.1955	2	17.11.20	0	15	07.07.2016	08.07.2016	2	.	4.76	18.07.2016	.	19.07.2016	06.07.2016	22.07.2016	RC
28		15.01.1957	2	18.01.20	0	15	21.07.2016	22.07.2016	2	.	3.06	03.08.2016		04.08.2016	20.07.2016	22.08.2016	CR
29		17.05.1956	1	24.12.20	0	15	28.07.2016	29.07.2016	2	.	4.52	08.08.2016	.	10.08.2016	27.07.2016	11.08.2016	1
30		30.01.1956	1	17.08.20	0	VP-16 MEL	11.11.2016	14.11.2016	2	.	4.68	23.11.2016	.	23.11.2016	09.11.2016	28.11.2016	2
31		30.09.1955	1	07.06.20	0	15	23.11.2016	24.11.2016	2	.	3.25	04.12.2016	.	08.12.2016	22.11.2016	15.12.2016	sCR
32		09.12.1943	1	19.12.20	0	6	05.01.2017	11.01.2017	2		3.81	25.01.2017		06.02.2017	04.01.2017	21.02.2017	2
33		22.05.1956	1	16.08.20	0	15	19.01.2017	20.01.2017	2		5.02	30.01.2017		02.02.2017	18.01.2017	04.02.2017	2
34		20.07.1963	1	16.08.20	0	15	09.03.2017	10.03.2017	2		3.25	21.03.2017		24.03.2017	08.03.2017	25.03.2017	
35		06.12.1973	1	20.02.20	0	6	16.03.2017	22.03.2017	2	.	2.87	04.04.2017		07.04.2017	15.03.2017	06.04.2017	2
36		12.01.1949	1	07.07.20	0	6	23.03.2017	27.03.2017	2	.	3.44	12.04.2017		13.04.2017	22.03.2017	19.04.2017	2
37		15.12.1966	2	29.11.20	0	10	28.03.2017	04.04.2017	2		3.14	15.04.2017		15.04.2017	27.03.2017	21.04.2017	2
38		02.06.1979	2	10.11.20	0	6	14.04.2017	20.04.2017	2		13.90	29.04.2017		29.04.2017	13.04.2017	03.05.2017	2
39		14.12.1975	2	01.07.20	0	CET	17.05.2017	23.05.2017	2		4.66	02.06.2017		05.06.2017	16.05.2017	09.06.2017	3
40		17.03.1953	1	20.03.20	0	6	18.05.2017	24.05.2017	2		6.06	02.06.2017		05.06.2017	17.05.2017	06.06.2017	3
41		11.02.1958	1	.10.201	0	6	08.06.2017	14.06.2017	2		5.15	24.06.2017		25.06.2017	07.06.2017	03.07.2017	2
42		18.01.1965	1	.06.201	0	15	22.06.2017	23.06.2017	2		4.19	03.07.2017		04.07.2017	21.06.2017	10.07.2017	2
43		22.01.1966	1	27.10.20	0	6	22.06.2017	28.06.2017	2		3.55	08.07.2017		12.07.2017	21.06.2017	12.07.2017	2
44		28.07.1956	1	13.10.20	0	6	20.07.2017	26.07.2017	2		2.71	06.08.2017		13.08.2017	19.07.2017	14.08.2017	2
45		17.11.1952	2	14.05.20	0	6	24.08.2017	30.08.2017	2		2.85	10.09.2017		20.09.2017	23.08.2017	18.09.2017	2
46		15.11.1955	2	30.03.20	0	15	31.08.2017	01.09.2017	2		4.38	11.09.2017		13.09.2017	30.08.2017	14.09.2017	sCR
47		05.05.1948	1	27.03.20	0	15	13.09.2017	14.09.2017	2		2.98	25.09.2017		28.09.2017	12.09.2017	03.10.2017	2
48		06.05.1948	2	04.05.20	0	6	19.10.2017	25.10.2017	2		3.52	03.11.2017		09.11.2017	18.10.2017	17.11.2017	2
49		08.08.1958	2	19.12.20	0	6	27.10.2017	03.11.2017	2		4.57	13.11.2017		15.11.2017	27.10.2017	21.11.2017	2
50		28.04.1968	1	28.05.20	0	6	16.11.2017	23.11.2017	2		5.21	01.12.2017		07.12.2017	15.11.2017	05.12.2017	2
51		01.12.1948	1	05.01.20	0	15	03.01.2018	04.01.2018	2		2.62	14.01.2018		17.01.2018	02.01.2018	18.01.2018	2
52		10.03.1955	1	12.09.20	0	6	18.01.2018	24.01.2018	2		6.53	02.02.2018		05.02.2018	17.01.2018	12.02.2018	2
53		21.02.1951	2	19.05.20	0	15	06.02.2018	07.02.2018	2		5.13	16.02.2018		19.02.2018	05.02.2018	01.03.2018	1
54		25.08.1968	2	02.03.20	0	6	02.02.2018	08.02.2018	2		2.22	-		-	01.02.2018	14.02.2018	exitus 14.02.2018
55		01.01.1958	1	27.03.20	0	15	08.02.2018	09.02.2018	2		3.04	19.02.2018		22.02.2018	07.02.2018	22.02.2018	2
56		30.06.1957	1	29.08.20	0	15	06.03.2018	07.03.2018	2		11.02	20.03.2018		21.03.2018	05.03.2018	22.03.2018	1
57		15.05.1954	2	18.09.20	0	15	15.03.2018	16.03.2018	2		3.11	26.03.2018		27.03.2018	14.03.2018	30.03.2018	sCR
58		18.04.1961	1	02.11.20	0	15	12.04.2018	13.04.2018	2		5.99	22.04.2018		25.04.2018	11.04.2018	25.04.2018	4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RACK: Torre B
RACK: Torre C
RACK: Torre D
TANK: Bidone azoto
PIANO: Sopra
PIANO: Sotto
POSIZIONE: 1
POSIZIONE: 2
POSIZIONE: 3
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POSIZIONE: 4
H016118000352
POSIZIONE: 5
POSIZIONE: 6

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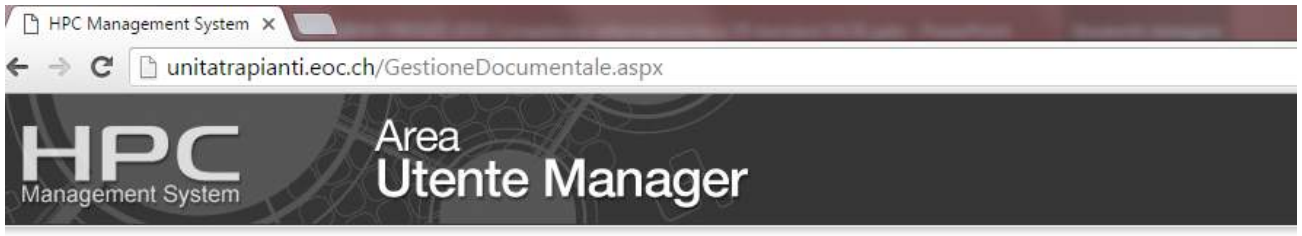
VISUALIZZA REINFUSIONI

Codice: Cognome: Tipo trapianto: Data dal: Data al: Provenienza: Tutte Conferma

DATA REINFUSIONE	CODICE UNITA	FRAZIONE N°	TIPO TRAPIANTO	TIPO	PROVENIENZA
25/10/2018 13.10.00	H01611800045	1	AUTOLOGO	HPC-A	Interna
20/06/2018 12.07.00	H01611800031	1	AUTOLOGO	HPC-A	Interna
22/05/2018 15.00.00	H01611800021	1	AUTOLOGO	HPC-A	Interna
07/03/2018 12.00.00	H01611800009	1	AUTOLOGO	HPC-A	Interna
19/01/2018 11.05.00	H01611700002	1	AUTOLOGO	HPC-A	Interna



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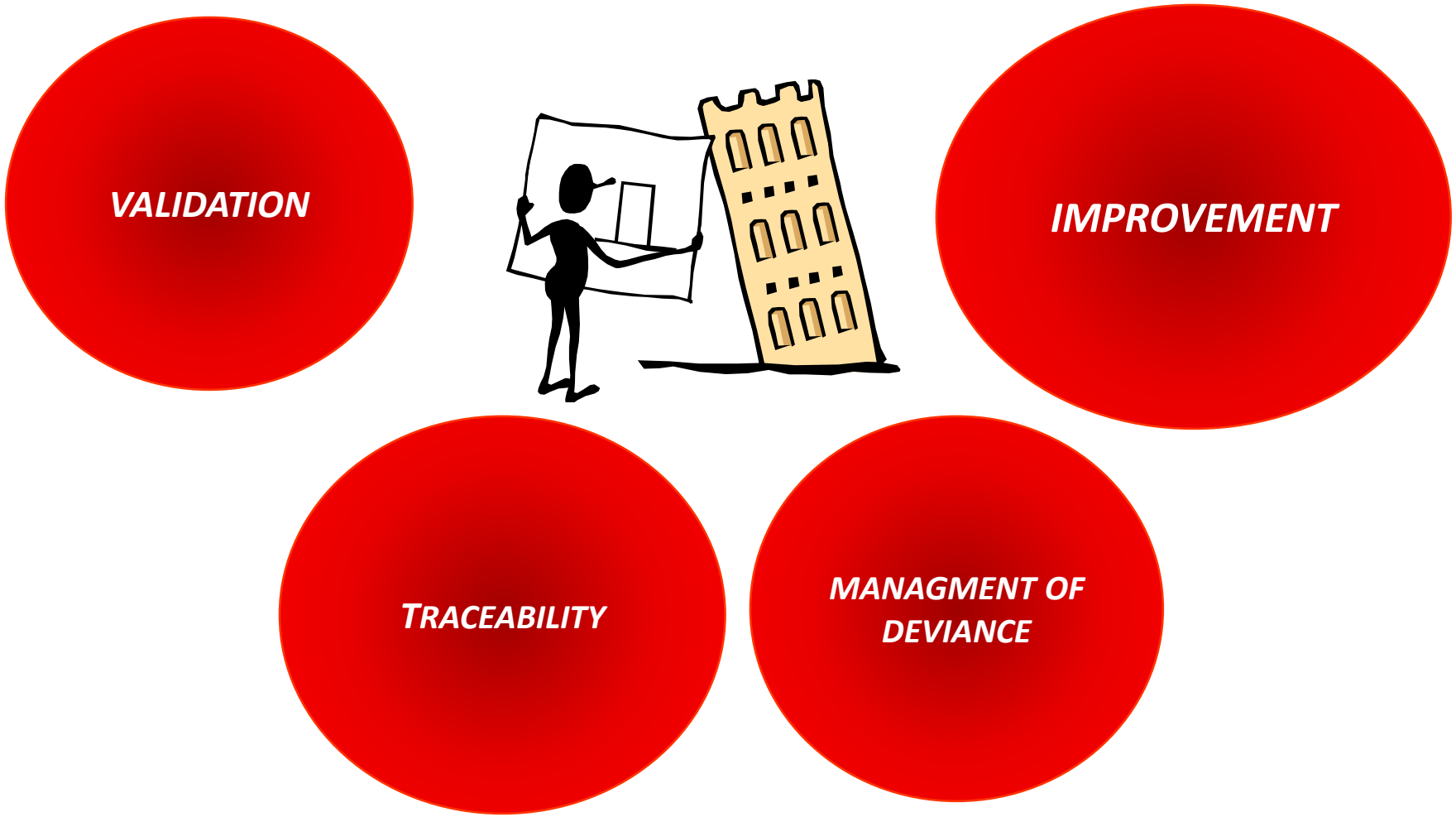
Qualità
Gestione EIEA
Gestione azioni correttive

SOPS = Safety

SOPS WRITING MEANS MORE SECURITY IN TERMS OF



	A	B	C
43	I-UT-038 (non più in uso)	Domanda di garanzia di presa a carico dei costi per trapianto di cellule staminali	09.06.2008 15.04.2010 rev
44	**I-UT-039/A**	Pulizia e manutenzione separatore cellulare Spectra Optia; Pulizia carrello e armadio LAF, controllo materiale per LAF e PBSCT; Pulizia locali (camere e uffici)	01.01.2017
45	**I-UT-040/D**	Inserimento e aggiornamento dei dati nel database dell'Unità Trapianti	01.01.2017
46	**I-UT-041/A**	Approvigionamento e deposito materiale ad uso specifico per l'Unità Trapianti	01.01.2017
47	**I-UT-042/B**	Programma vaccinazioni post-trapianto di cellule staminali autologhe	07.06.2018
48	**I-UT-043/A**	Fisioterapia per pazienti con trapianto autologo di cellule staminali periferiche	01.01.2017
49	**I-UT-044/C**	Valutazione dell'idoneità dei pazienti per l'ammissione nel programma trapianti	01.01.2017
50	**I-UT-045/B**	Diagnosi e gestione della cistite emorragica	01.01.2017
51	**I-UT-046/B**	Diagnosi e gestione delle complicazioni polmonari	01.01.2017
52	**I-UT-047/B**	Diagnosi e trattamento del "Graft Failure"	01.01.2017
53	**I-UT-048/E**	Gestione delle urgenze: disponibilità del medico di picchetto di Oncologia e accesso al Servizio di Medicina intensiva	01.01.2017
54	**I-UT-049/B**	Informazioni per i pazienti sul trapianto autologo di cellule staminali ematopoietiche	01.01.2017
55	**I-UT-050** (non piu' in uso)	Come prepararsi al trapianto allogenico: Informazioni per pazienti e familiari, come affrontare al meglio il ricovero a Basilea	06/2010 11/2013 rev
56	**I-UT-051**	Sorveglianza delle complicanze tardive legate al trapianto autologo di cellule staminali periferiche	01.01.2017
57	**I-UT-052**	Iter paziente nello studio clinico	01.01.2017
58	**I-UT-053**	Gestione del prodotto di leucoaferesi deviato	01.01.2017
59	**I-UT-054/B**	Gestione delle leucoaferesi in regime ambulatoriale	01.01.2017
60	**I-UT-054**	allegato	16.08.2017

ISTRUZIONI | MODULI UT | DIRETTIVE | MQ e PROCESSI

Nurse Training

- For nurses who operates in Jacie setting, training is not limited to continuous adjournment only
- Competencies must be defined and verified annualy
- Provision for continous annual education must be evidenced and traiced for each nurse.

- Adequate knowledge of the scientific and technical processes
- Awareness of the organizational framework, quality system and safety environment of the Unit
- Adequate knowledge of legal and ethical principles, including regulatory concepts of their work

Training and Retraining

- Internal educational and courses
- Participation on external educational events
- Retraining

Competences development

- Focus Groups
- Clinical case discussion
- Implementation of changes (for what purpose, what impact it can have ..)
- Observation of practice
- Presentations or publications
- SOPs review
- ……

Information Management

- Information sharing / diffusion
- Briefing
- Structuring opportunities for sharing

Document Management

- CV adjournment
- CME, courses
- Database
- Portfolio
- Meeting minutes

Professional Competencies

STANDARD:

C4.3 The Quality Management Plan shall include, or summarize and reference, personnel education, experience, and training requirements for each key position in the Apheresis Collection Facility. Personnel requirements shall include at a minimum:

C4.3.1 Current job description for all staff.

C4.3.2 A system to document the following for each staff member:

C4.3.2.1 Initial qualifications.

C4.3.2.2 Orientation.

C4.3.2.3 Initial training.

C4.3.2.4 Competency for each critical function performed.

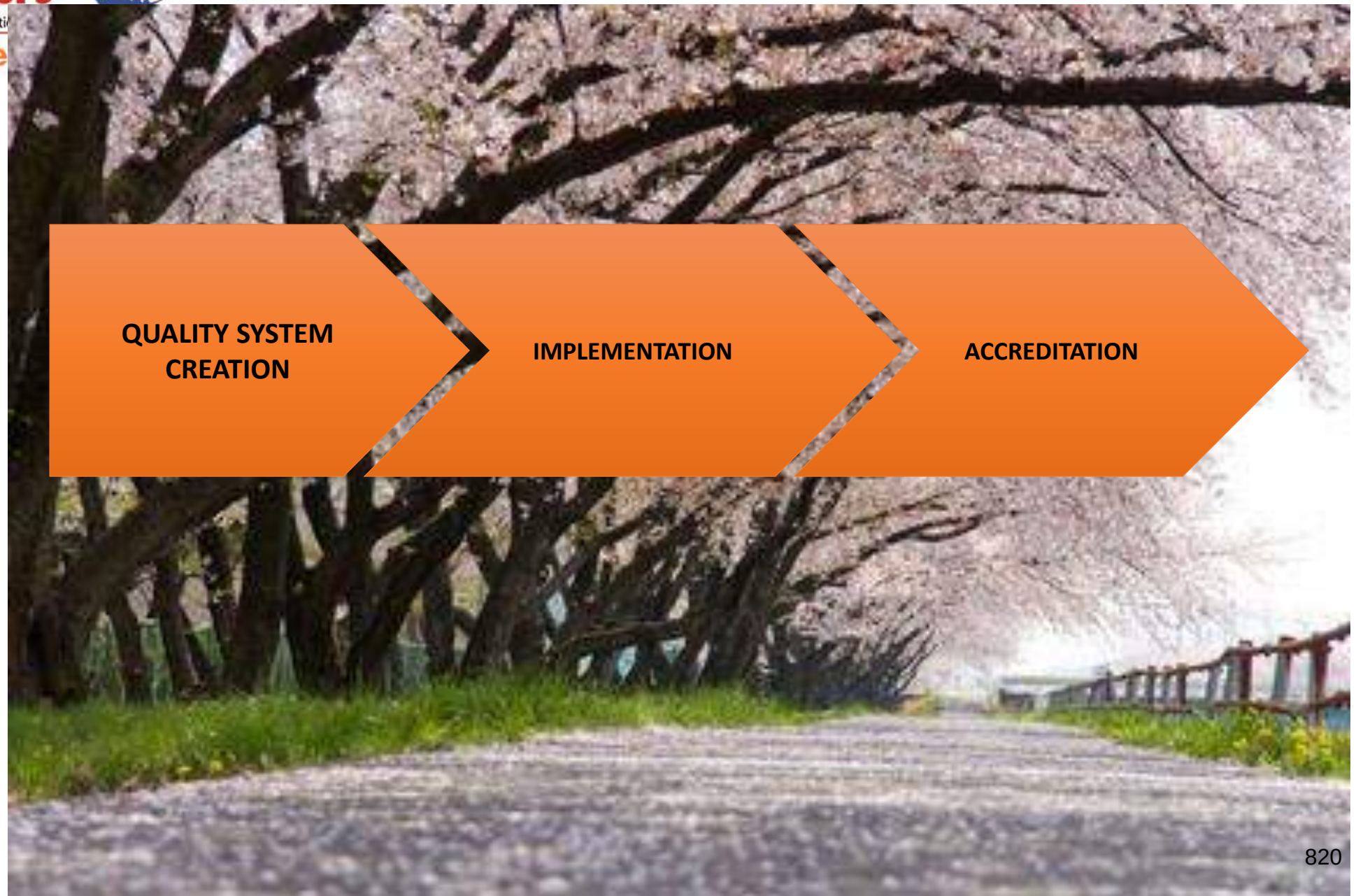
C4.3.2.5 Continued competency at least annually.

C4.3.2.6 Training and retraining.

C4.3.2.7 Provisions for continuing education.

C4.3.3 A description of minimal trainer qualifications and a uniform plan for staff training.

QM vs accreditation journey - summary



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QM vs accreditation journey - summary

QM vs accreditation journey - summary