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Donor safety including minors as donors

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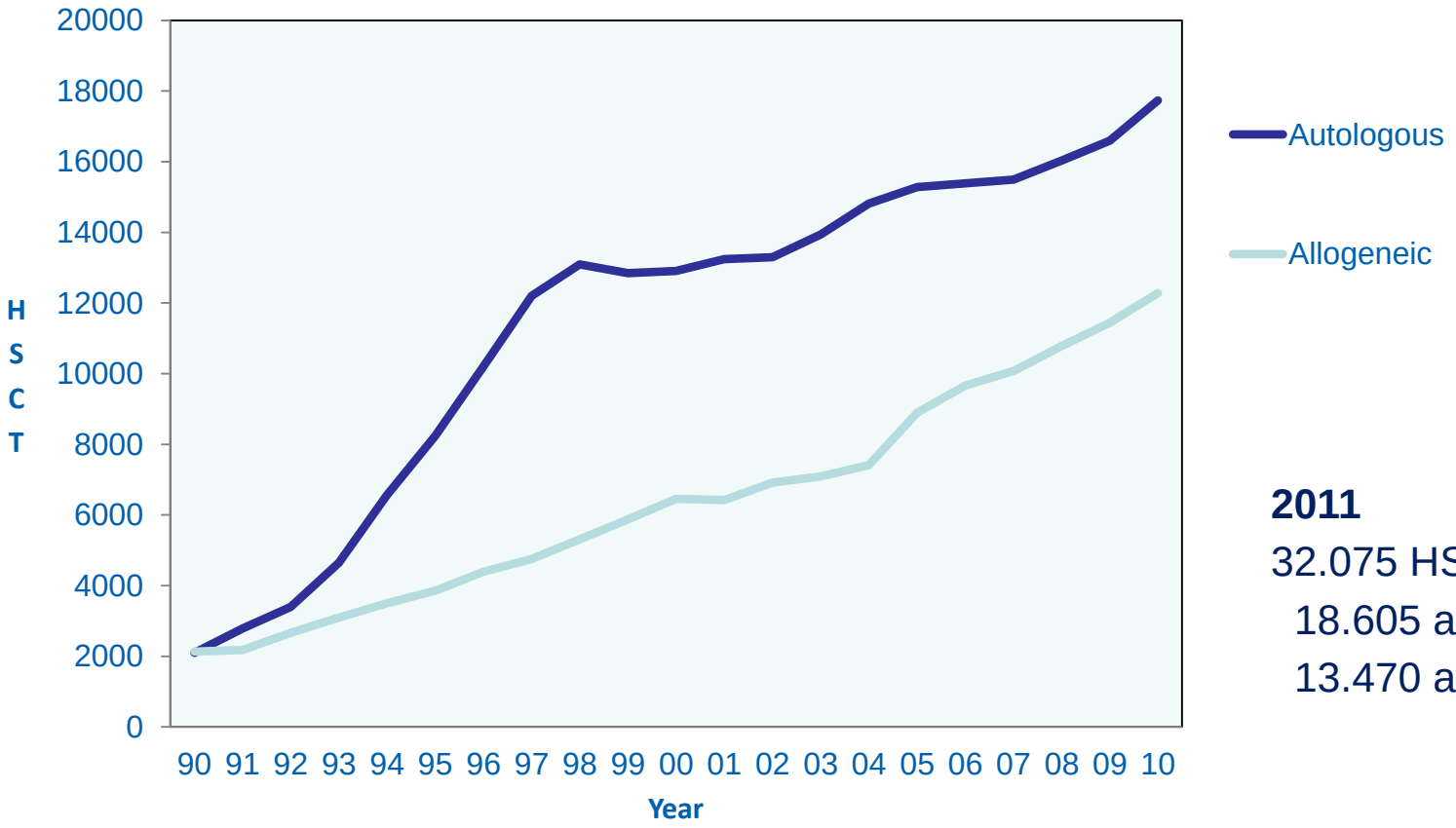
Blood stem cell transplantation: a success story



2011

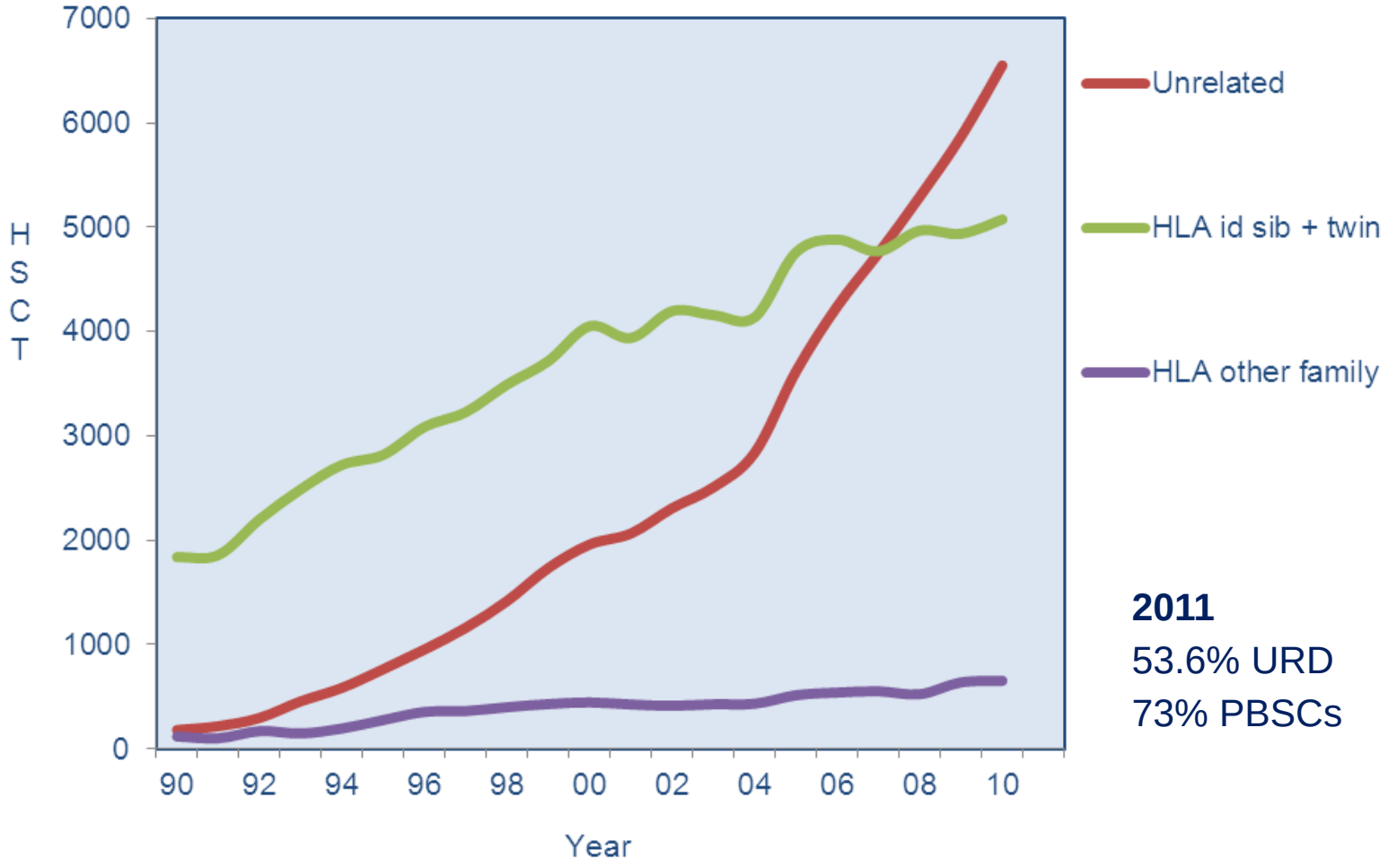
32.075 HSCTs

18.605 autologous

13.470 allogeneic

EBMT activity survey 1990-2011 Passweg JR et al. BMT 2012

Donor origin 1990-2010



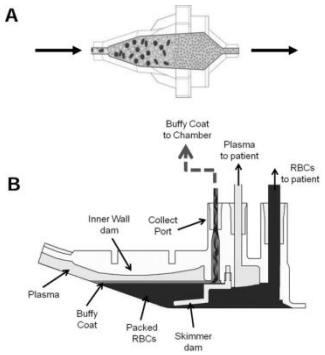
2011

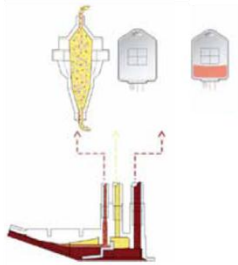
53.6% URD

73% PBSCs

EBMT activity survey 1990-2010 Passweg JR et al. BMT 2012

Peripheral blood stem cell collection

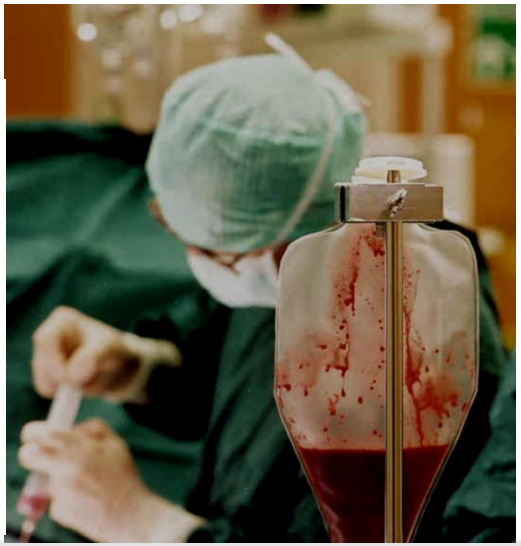




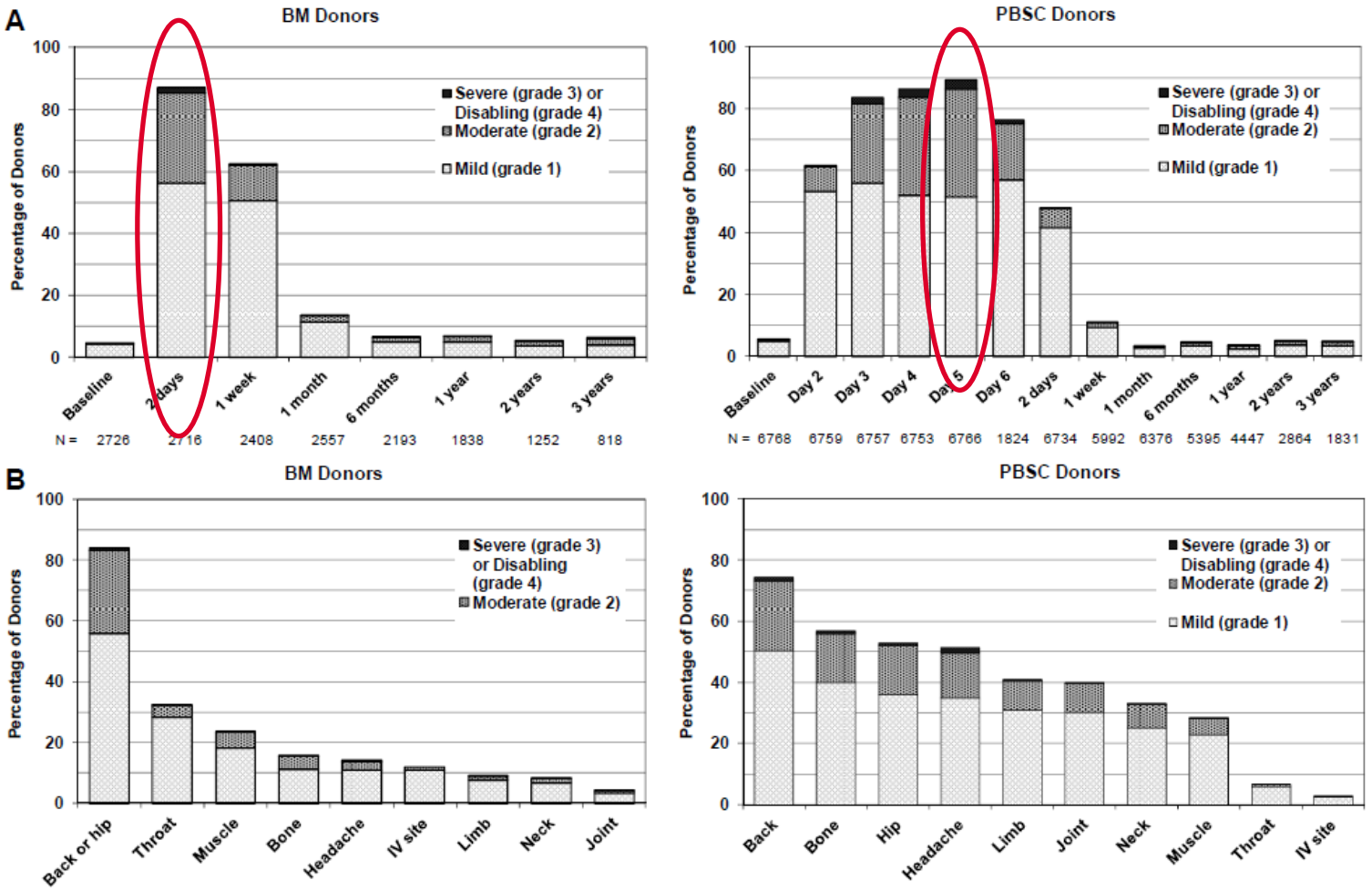
- From mobilised donors: G-CSF (plerixafor)
- Using cell separators – mostly continuous
- Duration 4-6 hrs
- Low-density MNC drawn from a dynamic interface between RBC and plasma

Bone marrow harvest

- Performed under GA with donor prone
- Marrow aspirated from both iliac crests
- Maximum 20mL/kg, 150 min anesthesia
- Passed into bag with anticoagulant
- Filtered to remove debris & larger particles



Acute toxicities: URD BM vs PBSC donation



Pulsipher M. et al., Blood 2013

Fatal events in temporal association with donation procedure

	BM	PB	published
EBMT	1 PE (38yrs)	1 error (27yrs) 1 SDH (67yrs) 2 cardiac (43,52yrs)	J. Halter 2009
US			Horowitz 2005
JSHCT	(1) CNS	0	0
South America		1 intracerebral bleeding	abstract
WMDA		1 hemato-pneumothorax	alert

risk: 1:10‘000 – 1:20‘000 donations ?

→ Causality? Risk factors?

Serious adverse events during and shortly after the donation procedure

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Donation of peripheral blood stem cells:

- Associated with G-CSF
  - allergic reactions, anaphylaxis, splenic rupture, respiratory problems, exacerbation of inflammatory diseases, thrombosis, sickle cell crisis
- Associated with a catheter
  - bleeding, thrombosis, tissue injury
- Associated with apheresis procedure
  - signs of low blood calcium, low platelet count

Hölig et al. Blood 2009, Kodera et al. EBMT 2008, Miller et al. BBMT 2008, Pulsipher et al. Blood 2009 and Blood 2013
Halter et al. Haematologica 2009, Confer DL. Hematology 2009 & NOTIFY 2011, Styczynski J et al.Blood 2012

Serious adverse events during and shortly after the donation procedure

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BM donation:

- Associated with anaesthesia:
  - cardiac or lung problems, hyperthermia, serious allergic reaction
- Local complications from puncture sites:
  - infection, bleeding, tissue injury
- Need for blood transfusion from allogeneic donors

True frequency unknown, but less than 1‰ (depends on definition of a serious adverse event)

Hölig et al. Blood 2009, Kodera et al. EBMT 2008, Miller et al. BBMT 2008, Pulsipher et al. Blood 2009 and Blood 2013
Halter et al. Haematologica 2009, Confer DL. Hematology 2009 & NOTIFY 2011, Styczynski J et al.Blood 2012

Incidence of severe/serious adverse events

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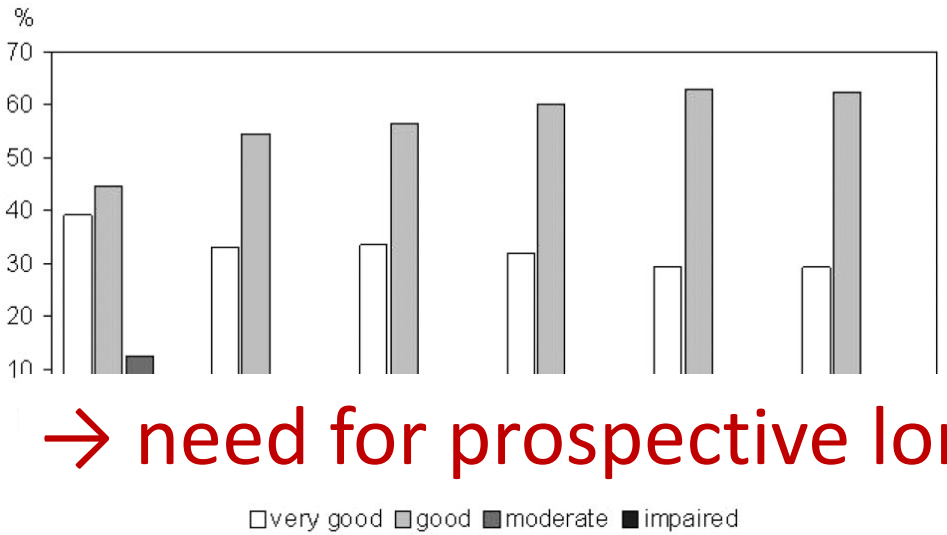
	DKMS	JSHCT	NMDP	EBMT	EBMT ped
design	prospective	prospective	prospective	retrospective	prospective
n BM n PB	-- 3.928	5.921 3.264	9.245 7.850	27.770 23.254	313 140
BM	--	0.37%	1.35%	0.04%	--
PB	<0.1%	0.61%	0.5-0.6%	0.11%	0.7%

Hölig et al. Blood 2009, Kodera et al. EBMT 2008, Miller et al. BBMT 2008/ Pulsipher et al. Blood 2009, Halter et al. Haematologica 2009, Styczynski J et al.Blood 2012

Late effects



General health status by self-assessments of PBSC donors (unrelated, n=3928).

→ need for prospective long term follow up!

Malignancies:

- Initial concerns were not confirmed by recent studies
- No increased risk so far for hematological or other neoplasias
- Large numbers needed for final analysis

Autoimmunity?

Others?

Hölig K et al. Blood 2009

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]

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WBMT WWW.WBMT.ORG

- Recommendations for a minimum data set for prospective donor follow-up were developed
- Report on donation procedure and up to 30 days after (start with 1st G-CSF, the start of anesthesia or the start of apheresis).
- Long term follow up report after last donation: after 1 year has elapsed from the date of the procedure.
- After that, annual or biannual follow-up encouraged. Minimum submission should be after 5 years and again after 10 years

Halter J, BMT 2013

Suitability criteria for pediatric donors, elderly donors and donors with health disorders

3rd Donor Outcome Workshop

September 12 and 13, 2013

Vienna, Austria

Eligibility criteria	Group leader	Group
Musculoskeletal and autoimmune disorders, immunodeficiencies, allergies, eye diseases, endocrine and metabolic diseases	Hans Hägglund	Vanessa Hala, Gerda Leitner, Thilo Mengling, Tigran Torosian
Disorders of the lung, GI-tract liver (excl. viral hepatitis), kidney, neurological, psychological, psychiatric disorder, unexplained fatigue syndrome	Andreas Buser	Mats Bengtsson, Nataliya Gerdt, Valeria Giudice, Kristina Hölig, Barbara Schultes
Hematological and oncological diseases (incl MGUS, MBL), malignancies	Willis Navarro	Mirjam Fechter, Vanessa Hala, Thilo Mengling, Tanja Netelenbos, Marta Torrabadella
Cardiovascular, cerebrovascular, and peripheral vascular diseases	Hildegard T Greinix	Mats Bengtsson, Annelies Billen, Mirjam Fechter, Valeria Giudice, Kristina Hölig, Vanderson Rocha Anne-Marie van Walraven,

Medical health history and evaluation in related donors

- Personal history, including allergi… experience with anesthesia
- Few laboratory parameters (I… globinopathies)
- Exercise tolerance
- Neurologic, cardiovas… atory or musculosceletal problems
- Back pain or lower extr… pain

Short questionnaire before HLA typing !!

- Physical examination, including blood … ressure and pulse
- ECG
- Complete Blood Count
- Serum creatinine concentr…
- Pregnancy test
- Chest x-ray for pati… years or those with suspected cardiac or pulmonary diseas…
- CT scan?
- Myocard perfusion imaging?

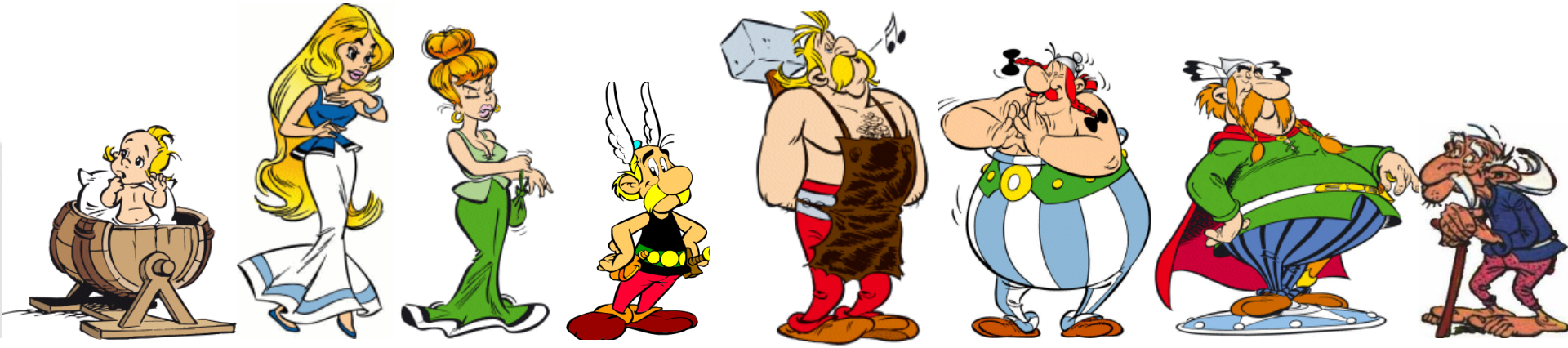
Detailed examination before HLA typing ??

Special issues: related donors

- Related donors are a much more heterogeneous population than unrelated donors with some presumably especially vulnerable subgroups as children, elderly or donors with comorbidities

- Considerable amount of related donors would be deferred from unrelated donations

Wiersum-Osselton J et al. EBMT 2009



Older PBSC donors

- Lower CD34+ counts/yields in PB and apheresis products
- Apheresis procedure complications increased [29 vs 15%]
- May need more days of collection, more mobilization failures
- More pain, slower recovery
- But: no evidence of worse recipient outcomes or safety issues for the donors

Lysak D, Clin Apheresis 2011; Richa E, BBMT 2009; Pulsipher MA Related donor Safety study, Tandem Meeting 2014

General considerations adult donors

- A related donor not meeting eligibility criteria for unrelated donors might be considered suitable for donation after careful **risk assessment** of donor's and recipient's risk.
- Donor selection and health assessment should be started **early** and efficient to provide basis for decision on donor suitability considering risks for donors and recipients.
- Providers responsible for donor care **should not** be involved in recipient's care.

General considerations pediatric donors

- To protect pediatric donors from rare situations when their psychological or medical health may be at risk, **advocacy** and **careful** medical review is recommend.
- Potential sibling donors with medical or psychological reasons not to donate should **not** be HLA typed.
- Donors with medical conditions should be **carefully** examined by skilled professionals, and if the risk of complication with collection is increased they should be deferred.

Conclusion

- Side effects and risks for donors are well defined and are **minimal**, related donors may be willing to accept greater risks.
- Consider **alternatives** early, if a donor presents with increased risk factors to avoid a delay in transplantation.
- Need for **international registries** to collect short- and long term medical (and psychological) data to improve our knowledge on risk assessment for HPC donation.

WBMT group

- **Jörg Halter**
- Derwood Pamphilon
- SBSC (CH): G. Nicoloso de Faveri, Python
- Leiden (NL): A.M. van Wa[illegible] Oudshorn, M. Fechter
- NMDP (USA): D. C[illegible] Navarro, M. Pulsipher
- JSHCT (JP): Y. Kode[illegible]a, K. Miyamura

Thank you!