臍帶血移植目前的研究與未來的應用

A GIFT OF NATURE

長庚兒童醫院
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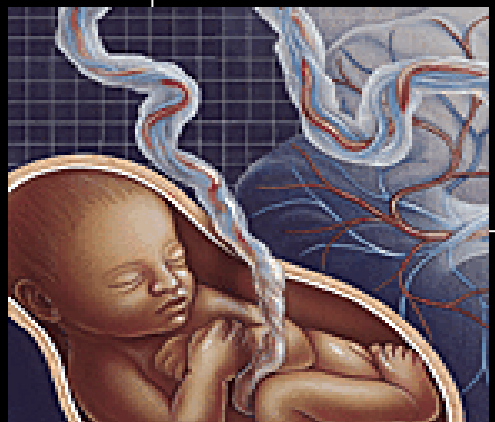
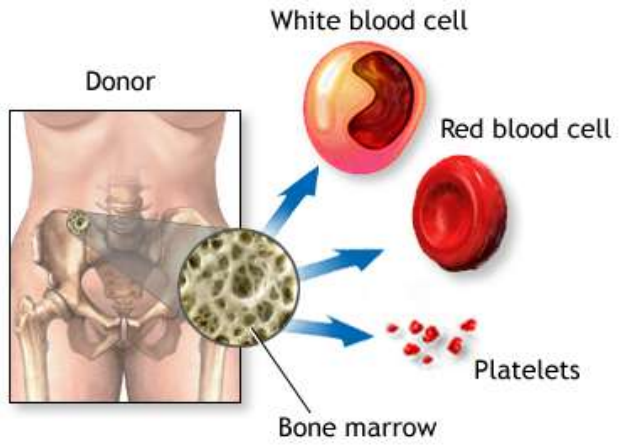


長庚兒童醫院
Chang Gung Children's Hospital

Advantages and Disadvantages of Embryonic Versus Adult Stem Cells

	Embryonic Stem Cells	Adult Stem Cells
Advantages	Highly expandable	Easily obtainable
	Pluripotent	No ethical objections
		Different expansion ability
		Uni-, bi-, multi- or pluripotent
		Highly compatible
		Autologous transplantation, no immune-suppressive therapy necessary
		Clinical application already realized
Disadvantages	Ethical objections	Lack of specific identification markers
	Difficult to isolate	
	Risk of rejection	
	Immune-suppressive therapy required	
	Arrhythmogenic potential	
	High risk of teratocarcinomas	
	Clinical application not feasible for 10 to 20 years	
	Lack of specific identification markers	



Stem-Cell Transplantation

- **Autologous (from the patient)**
- **Syngeneic (identical twin)**
- **Allogeneic (donated by another individual)**

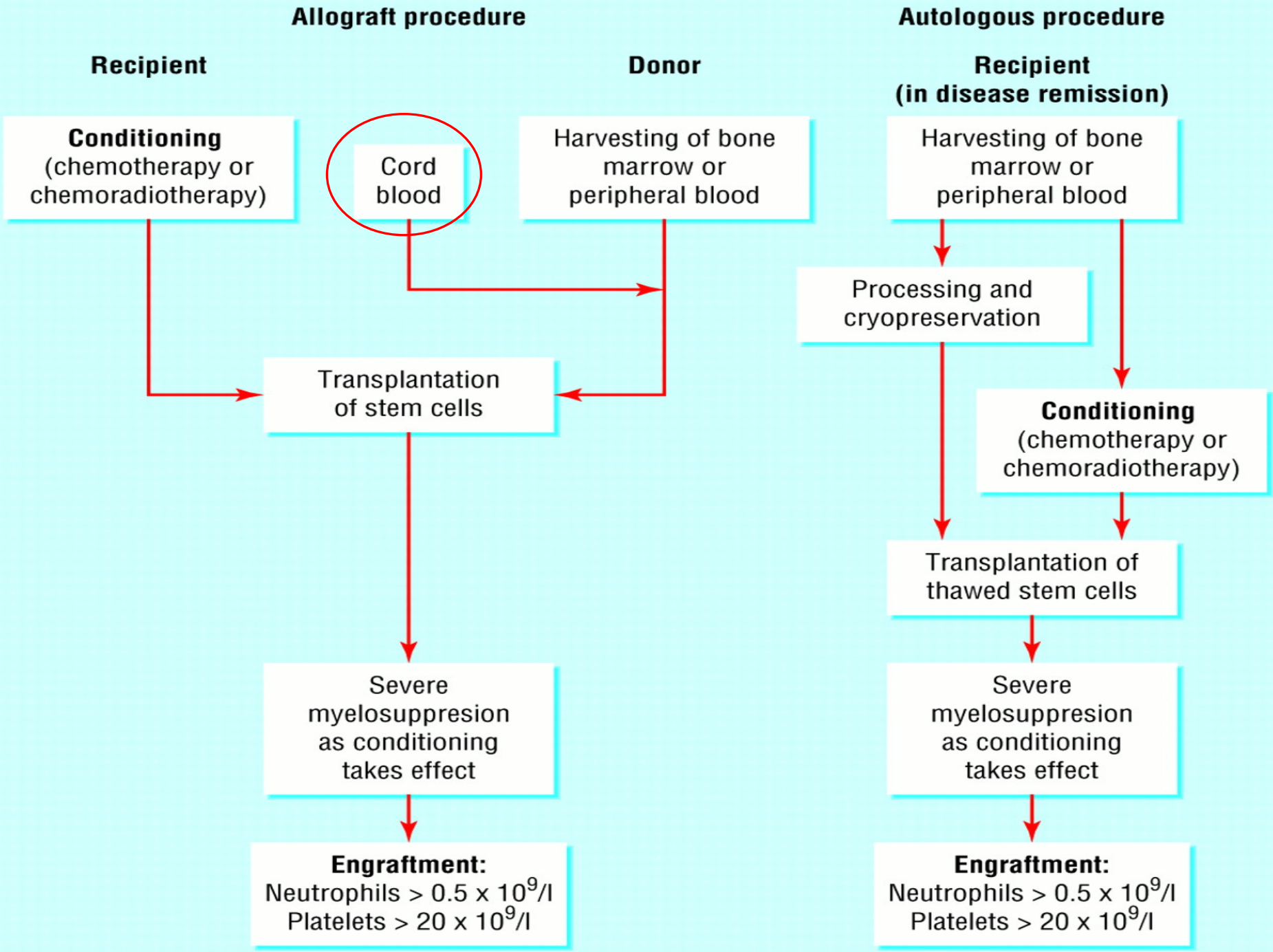
- **Bone marrow (BMT)**
- **Peripheral blood progenitor cell (PBPCT)**
- **Umbilical cord blood (UCBT)**

Stem Cell

- Totipotent
- Pluripotent
- Multipotent

- “全能”幹細胞 (4-8 cells)
- “萬能”幹細胞 (> 8 cells)
- “多能”幹細胞 (成體幹細胞)

	Cord Blood	Bone Marrow	Peripheral Blood Stem Cell
Volume	99 ml (50-360)	15-20 ml/kg	50-300 ml
Nucleated cells	$4.7 - 4.6 \times 10^8$	-	-
	3.7×10^7/kg (0.7-30)	$2-3 \times 10^8$/kg	$5-10 \times 10^8$/kg
CD34 cells	2×10^5/kg (0-45)	2×10^6/kg	$>5 \times 10^6$/kg
CFU-GM	$5-60 \times 10^5$		
	2.4×10^4/kg (0-222)		$>4 \times 10^5$/kg


Allograft procedure
Autologous procedure
Recipient
Donor
Recipient
(in disease remission)
Conditioning
(chemotherapy or
chemoradiotherapy)
Cord
blood
Harvesting of bone
marrow or
peripheral blood
Harvesting of bone
marrow or
peripheral blood
Processing and
cryopreservation
Transplantation
of stem cells
Conditioning
(chemotherapy or
chemoradiotherapy)
Transplantation of
thawed stem cells
Severe
myelosuppresion
as conditioning
takes effect
Severe
myelosuppresion
as conditioning
takes effect
Engraftment:
Neutrophils > 0.5 x 10^9/l
Platelets > 20 x 10^9/l
Engraftment:
Neutrophils > 0.5 x 10^9/l
Platelets > 20 x 10^9/l

Allogeneic Hematopoietic Cell Transplantation (HSC)

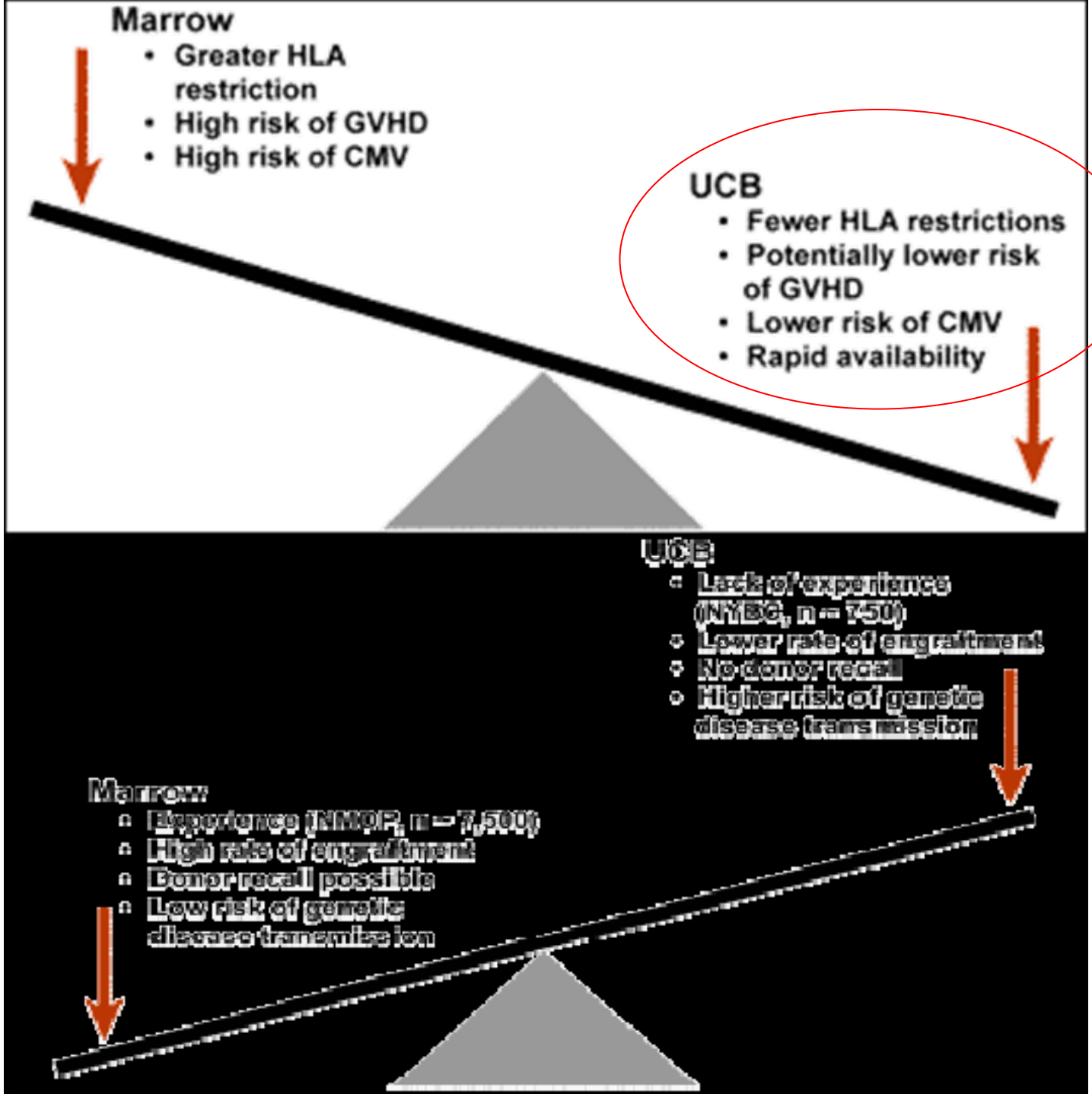
1. **Severe graft-versus-host disease (移植物抗宿主疾病)**
2. **Prolonged immuno-incompetence with high risk of opportunistic infection**
3. **Shortage of suitable donors, particularly for racial/ethnic minority patients**

Cord blood used as source of transplantation of hematopoietic stem cells

History of umbilical cord blood transplantation

- Wagner and colleagues stated that "The use of umbilical cord blood as a source of transplantable hemopoietic stem cells was first suggested in the early 1980s"

- Transplantation of UCB was successfully performed for the first time in 1988 to treat a boy with Fanconi's anemia; the donor, the boy's newborn sister, was a perfect HLA match for her brother. *(Gluckman et al, N Engl J Med 1989)*


Marrow
• Greater HLA restriction
• High risk of GVHD
• High risk of CMV
UCB
• Fewer HLA restrictions
• Potentially lower risk of GVHD
• Lower risk of CMV
• Rapid availability
UCB
Lack of experience (NYBC, n = 750)
Lower rate of engraftment
No donor recall
Higher risk of genetic disease transmission
Marrow
Experience (NMDP, n = 7,500)
High rate of engraftment
Donor recall possible
Low risk of genetic disease transmission

Umbilical Cord Blood Transplantation

- UCB should be considered when allogeneic transplantation is the treatment of choice for a child who does not have an HLA identical sibling, or a well matched unrelated donor.*(Sanz et al, 2001)*
- The optimal dose is about $2.0x10^7$ nucleated cells per kilogram of recipient body weight after thawing. Effectively, this means that most adults and larger children are not suitable recipients. *(Rocha et al, 2000; Gluckman, 2000)*

Disorders for which cord blood transplantation has been utilized as a treatment modality

- Acute lymphoblastic leukemia
- **Acute myeloid leukemia**
- Chronic myeloid leukemia
- Juvenile chronic myeloid leukemia
- Myelodysplastic syndrome
- **Severe combined immunodeficiency**
- Common variable immunodeficiency
- Kostmann's syndrome
- Neuroblastoma
- Wiskott-Aldrich syndrome
- X-linked lymphoproliferative d's
- **Hurler syndrome**
- Hunter syndrome
- **Fanconi anemia**
- Severe aplastic anemia
- **Cooley's anemia***
- Sickle cell anemia
- **Osteopetrosis**
- Adrenoleukodystrophy

If an unrelated UCB donor is considered (MT9118)

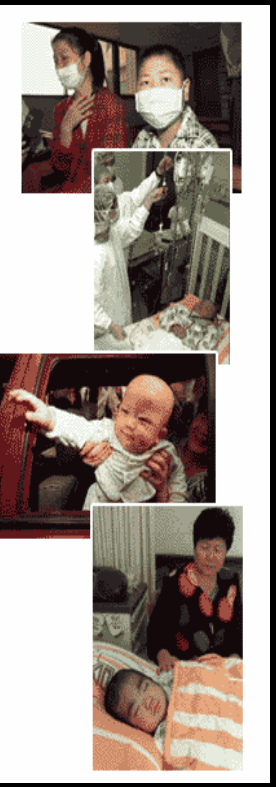
Patients with the following disease may proceed immediately to transplant

- ALL
- Secondary AML
- SCID
- Inborn error of metabolism
- Aplastic anemia
- Fanconi anemia
- Diamond-Blackfan anemia

Not to transplant until there is a search of the unrelated marrow donor registry

- **AML**
- **Wiskott-Aldrich syndrome**
- **CML**

Mucopolysaccharidoses

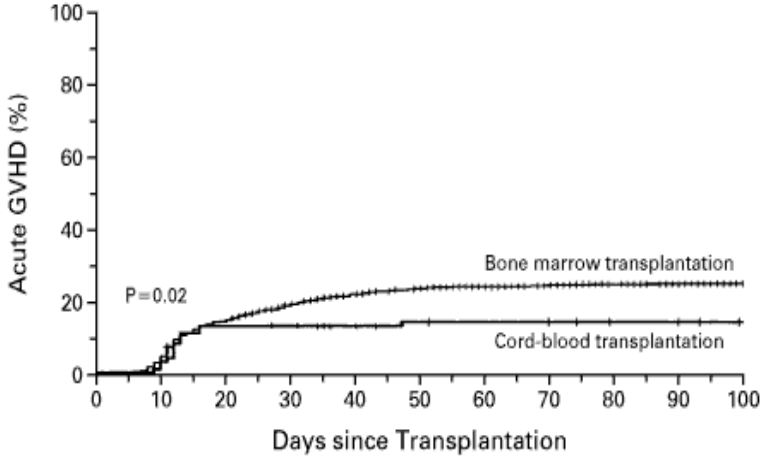


- MPS-I: Hurler's
- MPS-II: Hunter's*
- MPS-III: San Filippo*
- MPS-IV: Morquio*
- MPS-VI: Maroteaux
  -Lamy
- MPS-VII: Sly

* No reproducible clinical benefit and, therefore, are not advocated by most transplant centers.

- Residual complications such as BMT-engendered growth retardation and secondary malignancies despite correction of enzyme deficiency.
- Limited benefit occurs following transplantation in either the severe or mild forms of Hunter's syndrome. *(Peter et al 2000)*
- The lack of efficacy of HSCT in Hunter's syndrome is due to the fact the affected somatic cells do not take up the enzyme present in the plasma (iduronate sulfatase). *(Sullivan et al 2000)*
- Families may regret their decisions years from time of transplantation?

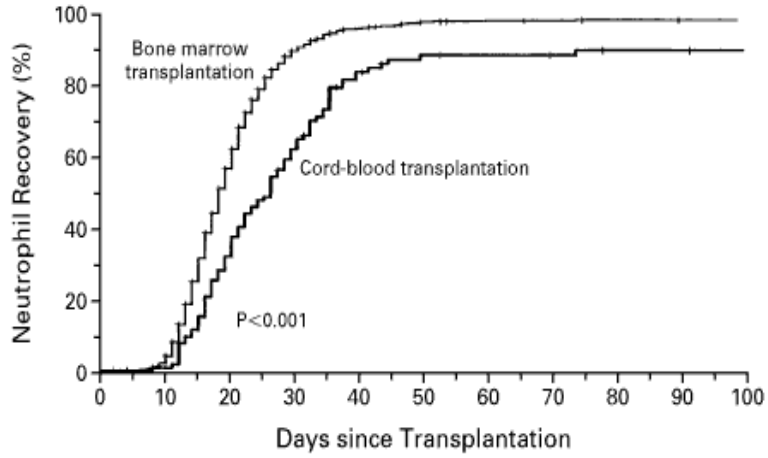
A



No. at Risk

Bone marrow transplantation	2012	1810	1597	1489	1422	1378	1350	1328	1311	1293	1260
Cord-blood transplantation	107	97	85	84	83	81	79	78	77	76	71

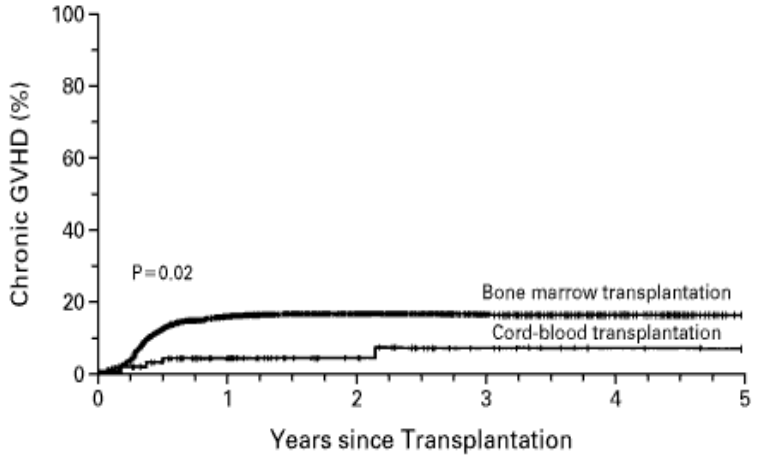
C



No. at Risk

Bone marrow transplantation	2018	71	60	40	37	33	30	29	29	27	26
Cord-blood transplantation	106	15	12	11	10	11	8	7	7	7	7

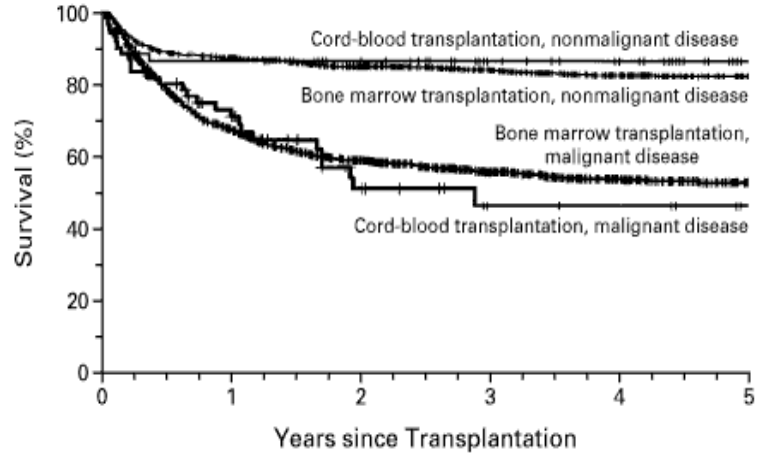
B



No. at Risk

Bone marrow transplantation	1779	1141	883	651	479	338
Cord-blood transplantation	93	61	36	18	8	5

D

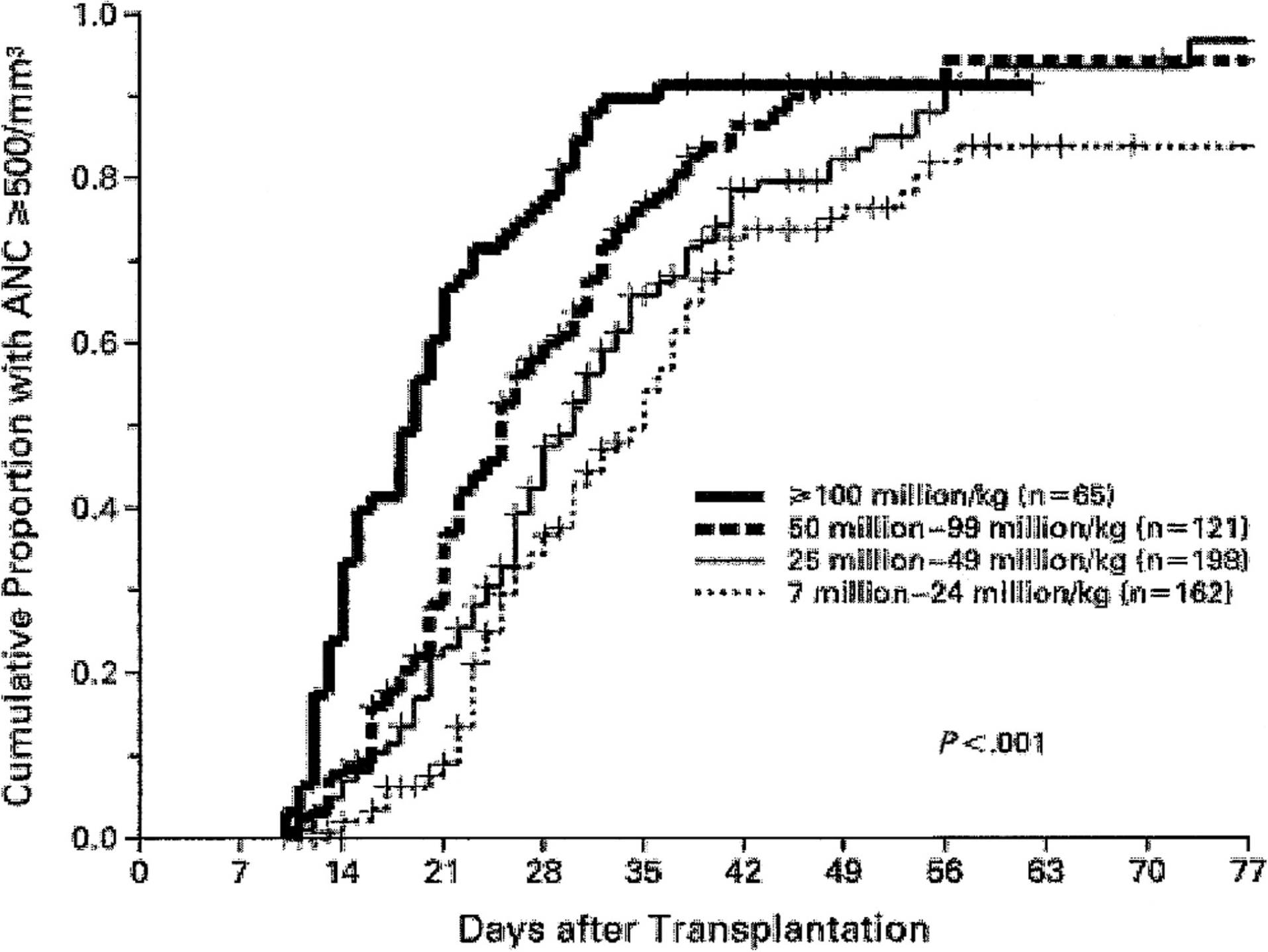


No. at Risk

Bone marrow transplantation, nonmalignant disease	789	644	530	419	333	252
Cord-blood transplantation, nonmalignant disease	52	37	26	13	5	2
Bone marrow transplantation, malignant disease	1263	763	570	409	284	186
Cord-blood transplantation, malignant disease	61	35	16	10	5	4

Status of umbilical cord blood transplantation → Young is better if enough

- Significantly less acute and chronic GVHD associated with the transplantation of HLA identical sibling cord blood compared with HLA identical sibling marrow; the immaturity of lymphocytes in cord blood dampens that reaction.*(Gluckman 2001; Anasetti 2001)*
- Although the clinical results are encouraging, UCB is associated with delayed engraftment.*(Fibbe et al, 2001)*
- UCB progenitor cells retaining a CD34+ phenotype after ex vivo expansion have less engraftment potential than do expanded CD34+ cells. *(Xu et al, 2001; Dravid et al, 2002)*

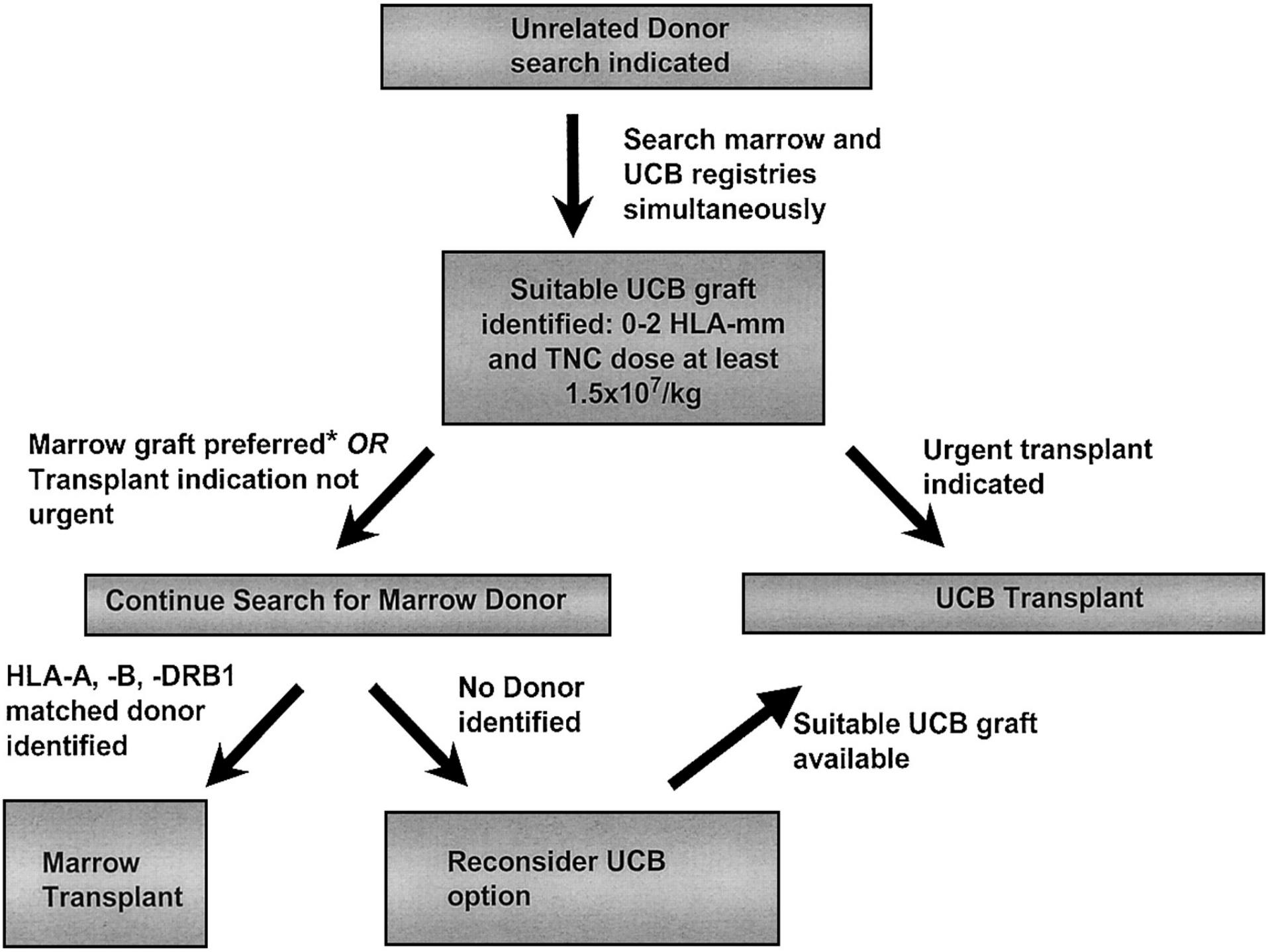

Cumulative Proportion with ANC ≥500/mm³
1.0
0.8
0.6
0.4
0.2
0.0
0
7
14
21
28
35
42
49
56
63
70
77
Days after Transplantation
≥100 million/kg (n=65)
50 million–99 million/kg (n=121)
25 million–49 million/kg (n=198)
7 million–24 million/kg (n=162)
P<.001

Advantages of Unrelated donor UCB

- Immediate availability
- Absence of donor risk and attrition
- Low risk of transmissible infectious diseases, such as CMV and EBV
- UCB T-cell naiveté protects from severe GVHD and that HLA matching criteria for selection of unrelated UCB may be relaxed.
- The ability to expand available donor pools in targeted ethnic and racial minorities currently underrepresented in all marrow donor registries

Choice of UCB graft

- Based primarily on **CD34 cell dose** and secondarily on degree HLA disparity
- At the University of Minnesota, local experience suggests that 1.5×10^7 nucleated cells/kg or 1.7×10^5 $CD34^+$ cells/kg define that threshold below which outcomes are significantly poor *(Wagner, 2002)*
- Recipients of $< 1.7 \times 10^5$ CD34/kg have slow hematopoietic recovery (median 35 days) and significantly lower incidence of engraftment (68%)
- The tolerability of HLA-2 antigen disparate grafts will likely increase the availability of HSC transplantation, particularly for patients with infrequent HLA haplotypes


Unrelated Donor search indicated
Search marrow and UCB registries simultaneously
Suitable UCB graft identified: 0-2 HLA-mm and TNC dose at least 1.5x10^7/kg
Marrow graft preferred* OR Transplant indication not urgent
Urgent transplant indicated
Continue Search for Marrow Donor
UCB Transplant
HLA-A, -B, -DRB1 matched donor identified
No Donor identified
Suitable UCB graft available
Marrow Transplant
Reconsider UCB option

Multi-unit UCB transplantation

- Private and publicly funded cord blood banks worldwide store an estimated **150,000** cryopreserved HLA-A–, HLA-B–, and HLA-DRB1–typed units, mostly for the purpose of URD transplantations *(Satkiran 2003)*
- Speeding engraftment after UCB transplantation, making a reasonable source of stem cells for adult recipients

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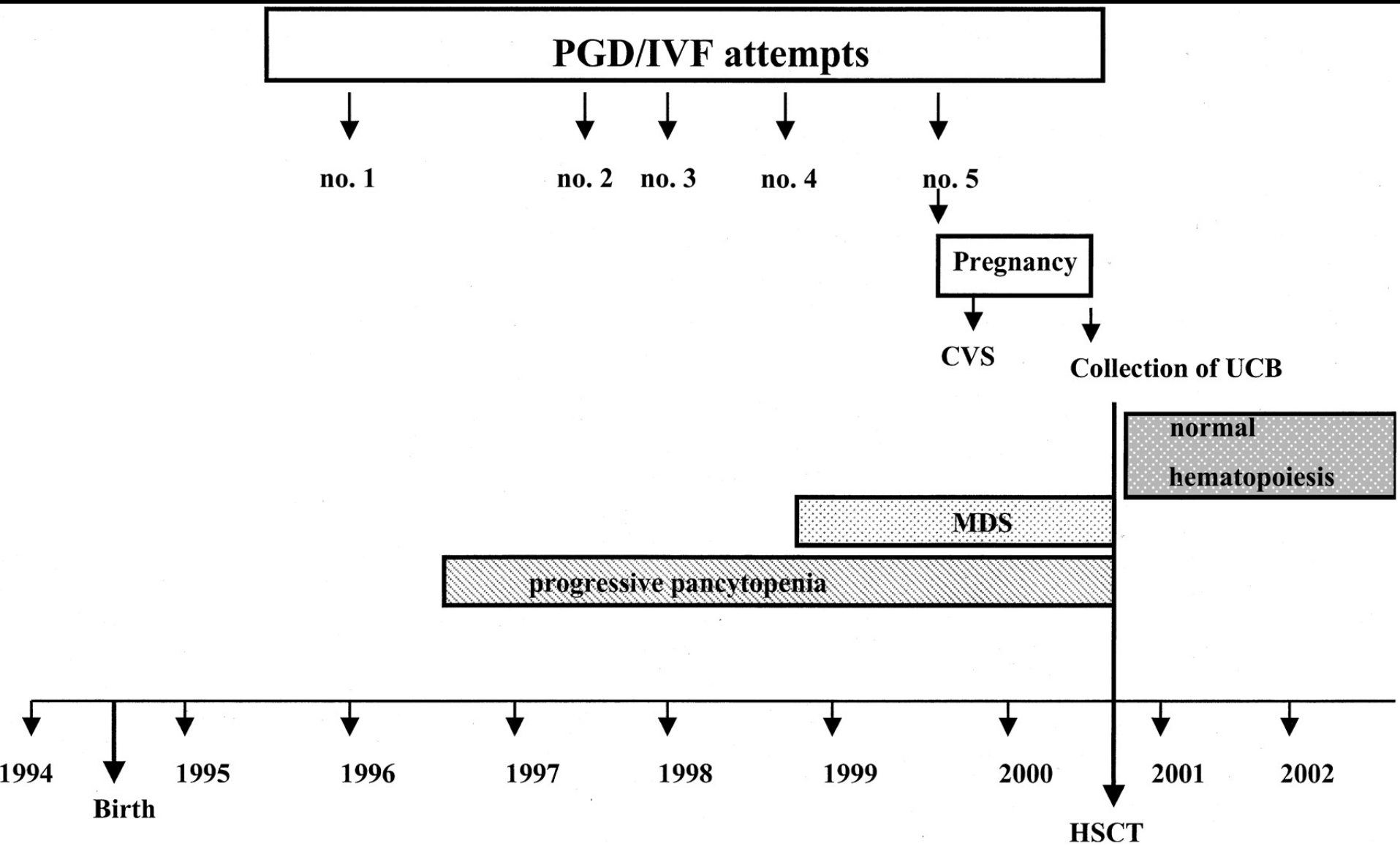
Preimplantation Genetic Diagnosis



Unresolved issues that will need to be addressed in the future

- Optimal methods for harvesting, processing, and storing UCB units
- Minimum number of banked UCB units necessary to support the needs of recipients who lack matched family member donors
- The minimum number of stem/progenitor cells required for hematopoietic engraftment in larger recipients
- The reported low incidence of GVHD after UCBT – might also be a major drawback in leukemic patients.
- Ex vivo expansion of UCB stem/progenitor cells; and immunologic reconstitution after UCBT

重型海洋性貧血病童應該接受臍帶血移植嗎?

長庚兒童醫院血液腫瘤科
江東和 醫師

Introduction

- The current conventional treatment of β-thalassemia major consisted of lifelong monthly blood transflusion combined with daily subcutaneous or oral iron chelation therapy.
- Hematopoietic stem cell transplantation with sibling BM or PB donors has long been used to cure thalassemia, first by Thomas and his colleagues at Seattle and most widely by Lucarelli's group and others in Italy.
- For those patients with a HLA-identical sibling, BMT offers a cure with excellent probability of thelassemia free survival if performed early (Lucarelli class I or II).

Umbilical Cord Blood (UCB)

- The use of UCB offers a potential means to alleviate the shortage of donors, especially that of ethnic minorities, that has plagues BMT since its inception.
- Unrelated CBT has rarely been used in the past due to the high graft failure and autologous recovery rates as well as unacceptable morality.
- “UCB transplantation have often been unsuccessful in the treatment of thalassemia because large numbers of transplanted cells need to be administered to sustain hematopoiesis and prevent rejection.”

History of umbilical cord blood transplantation for thalassemia major

- Transplantation of sibling cord-blood stem cells into a patient with severe thalassemia *(Issaragrisil et al. N Engl J Med 1995)*
- Unrelated umbilical cord blood transplant for beta-thalassemia major *(Fang et al. J Trop Pediatr 2003)*
- Unrelated peripheral blood and cord blood hematopoietic stem cell transplants for thalassemia major *(Tan et al. Am J Hematol 2004)*
- Successful unrelated cord blood transplantation in a child with beta-thalassemia major *(Jaing et al. J Trop Pediatr 2005)*

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Patients

- Transplanted from October 2003 to the patient accrual cut off date of February 2006
- Patients No.: 13 (M:F = 7:6)
- Age : 2.3-11.4 year (median 4.8 year)
- Body weight: 12.5-38 (median 17.5 kg)
- Pesaro class at time of CBT: all patients were class 1, except for two which was class 2
- No HLA-identical sibling donor or unrelated BM donor with 0-3 HLA mismatches to the recipients

Cord Blood Selection and Characteristics

- HLA-A, -B, and -DRB1 assessed by high-resolution PCR-SSP
- HLA compatibility : a minimum of 2 HLA antigens shared with the recipient was required *(rejection mm not included)*, and only 1 DRB1 mismatch was allowed.
- The selected cord blood had to contain, per kilogram of the recipient's body weight, at least 2 x 10^7 nucleated cells and 1.7 x 10^5 $CD34^+$ cells (determined at the time of cryopreservation).

Conditioning Regimen and Transplantation Procedure

- The preparative regimens consisted of oral busulfan 3.5 mg/kg/day (day –9 to –6), cyclophosphamide 50 mg/kg/day (day –5 to –2) and ATG 30 mg/kg/day (day –4 to –1).
- Direct thaw without removal of red cells
- Phenytoin for prophylaxis against seizures. Mesna 50 mg/kg on the days of cyclophosphamide infusion.
- GVHD prophylaxis comprised cyclosporine (2.5 mg/kg q8h) from day –3 with a course of methylprednisolone (1 mg/kg *i.v.* q12h on days 5 to 19, decreasing 25% thereafter every other day).
- Cyclosporine dose may be tapered beginning at least 60 days after demonstrating neutrophil engraftment and full donor chimerism by STR analysis.

Supportive Care

- Blood components given to maintain Hb and platelet values $>$ 8 gm/dL and 20 x 10^9/L, respectively.
- Intravenous Cefazolin for streptococcal prophylaxis and oral itraconazole for antifungal prophylaxis
- Acyclovir and oral Bactrim to prevent CMV reactivation and *Pneumocystis carinii* infection
- Preemptive ganciclovir therapy for evidence of CMV reactivation
- IVIG (500 mg/kg) given on day –6, +7, +21, +35, +56, +77, and +98 following UCB transplantation

Posttransplantation Follow-up

- CMV pp65 antigenemia assay
- Neutrophil engraftment: 3 consecutive days of ANC $\geq$ 0.5 x 10^9/L
- Transfusion independent: the last day of RBC transfusion
- Platelet engraftment: 7 consecutive days of a platelet count of $\geq$ 20 x 10^9/L maintained without transfusion
- Serial STR PCR: confirm the conversion from mixed chimerism to a predominantly donor profile on day +60, +90, +120, +180, +270, and +360, followed by quarterly for the second year and yearly thereafter
- Desferrioxamine to accelerate the clearance of body iron deposits in the subset of patients with heavy iron overload who achieved neutrophil engraftment

Results (1)

- One patient died of multidrug-resistant *S. mitis* sepsis at day +8 prior to the “expected” time to respond.
- One patient slipped in the bathroom. Although complete donor chimerism was achieved, he died of intracranial hemorrhage and its sequelae one month later .
- All remaining 11 patients are alive and exthalassemic with a median follow up time of 502 days (range 32-883 days) as of March 18, 2006.
- Ten patients with neutrophil engraftment showed full donor chimerism by day +21 and the remaining one achieved stable mixed chimerism (85.6% donor’s cells) by day +365 and is currently at day +477 post-transplant.

Results (2)

- Median pre-freeze TNC dose was 8.7 x 10^7/kg (range 4.8-15.0 x 10^7/kg), and median pre-freeze CD34+ cell dose was 4.1 x 10^5/kg (range 2.1-8.0 x 10^5/kg) of the recipient's body weight.
- The median times to neutrophil engraftment, RBC transfusion independence, and platelet engraftment were 14 (range 12-21 days), 35 (range 20-120 days), and 51 (range 45-119 days) days after transplantation, respectively.
- CMV reactivation was detected in 4 patients (patients 2,5,8, and 12) on posttransplantation day 27, 62, 28, and 63, respectively.

Results (3)

- According to the Minnesota grading and a consensus method, all surviving patients experienced grade I-II acute GVHD that resolved with treatment, with no extensive chronic GVHD.
- The median day to hospital discharge was day +78 (range 46-137 days).
- Desferrioxamine was resumed in only 3 patients (patient 5,10,12) during the early posttransplantation period.

Table 1. Main clinical and biologic characteristics of patient population

Table 1. *Main Clinical and Biologic Characteristics of the 5 Patients*

Variable	Patient 1	2	3	4	5*
Clinical					
Age (y)	3.7	2.3	3.6	5.8	11.4
Genotype	IVS II-654 and p28	Homozygous IVS 654	Homozygous IVS 654	IVS II-654 and codon 43	IVS II-654 and codon 41/42
Disease status	Lucarelli class I	Lucarelli class I	Lucarelli class I	Lucarelli class I	Lucarelli class I
Pretransplantation serum ferritin level (μg/L)	515	1583	2461	797	2125
HLA type					
Patient	A2, A24, B46, B48, DRB1 1312, 1501	A11, —, B4001, B46 DRB1 0406, 1501	A0203, A2402, B1501, B3802, DRB1 0406, 1602	A0207, A2601, B1301, B4601, DRB1 1202, —	A0201, A2402, B1525, B5801, DRB1 0301, 1405
Donor	A2, A24, B46, B48 DRB1 0403, 1501	A1101, —, B4001, — DRB1 0405, 1501	A0203, —, B3802, — DRB1 0403, 1602	A0206, A1101, B1301, B4601, DRB1 1202, —	A0207, A3303, (A0201, —) B5801, —, (5601, 5801) DRB1 0301, 1405 (0301, 1401)
UCB					
Nucleated cell dose ($\times 10^7$/kg)	8.78	11.83	9.03	4.15	3.25
CD34 cell dose ($\times 10^5$/kg)	2.48	2.43	3.75	2.97	2.31

IVS indicates intervening sequence.

*Double cord blood transplantation.

Characteristics of engraftment, GVHD grading, outcome, and chimerism

Table 2. *Characteristics of Engraftment, GVHD Grading, Outcome, and Chimerism*

Variable	Patient 1	2	3	4	5*
Days until					
ANC >0.5 × 10^9/L	17	12	14	12	12
RBC transfusion independence	34	37	27	45	22
Platelets >20 × 10^9/L	49	46	43	43	55
GVHD grade	I	II	I	II	III
Outcome	Transfusion independence	Transfusion independence	Transfusion independence	Transfusion independence	Transfusion independence
Days after transplantation	454	344	303	245	152
Day of the last chimerism	360	270	270	180	120
Chimerism analysis (% donor cells)	100	100	100	100	100

ANC indicates absolute neutrophil count; RBC, red blood cell.

*Double cord blood transplantation.

Our patients don't routinely undergo liver biopsy. Eleven patients were classified as class 1 and 2 (P't 10 & 12) as class 2 based on the presence of 0, 1, or 2 of the remaining two features of the Pesaro classification (*i.e.*, hepatomegaly and poor chelation).

Preliminary Conclusion (1)

- These results show that when cell dose is optimal, unrelated CBT may be a promising approach for the curative therapy of thalassemia major.
- 77% of the patients contain 1 to 3 HLA A-, B- and DR-mismatches
- Outstanding overall survival rate and thalassemia free survival rate (91%) and transplant-related mortality rate (9%).

Preliminary Conclusion (2)

- Our results demonstrated that unrelated UCB transplantation procedure is highly valuable for transfusion-dependent thalassemia.
- Not only the disease can be cured, but also the quality of life is greatly improved.
- It is clearly cost-effective when compared to conventional treatment with life-long blood transfusions and iron chelation therapy. However, continued monitoring is mandatory.


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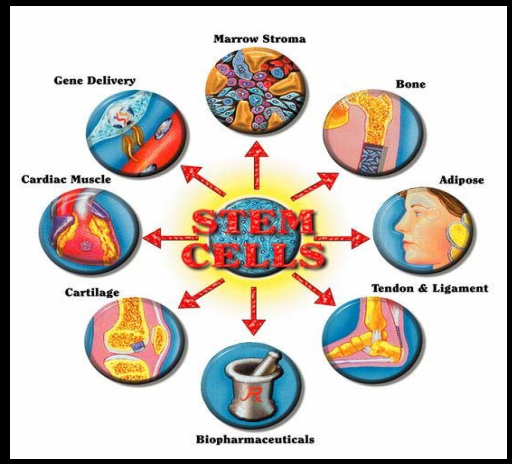
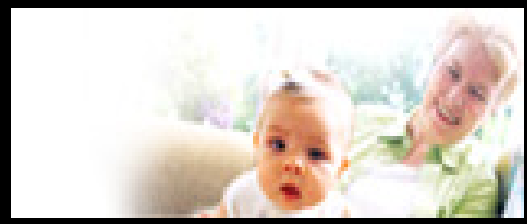
臍帶血幹細胞目前的研究和未來的應用



Stem cells from cord blood - current status and future potential

- **造血幹細胞移植 (HSCT)**
- 基因治療 (Gene therapy)
- 再生醫學 (Regenerative Medicine)



Indications for Allogeneic and Autologous Stem Cell Support

Disease	Allogeneic Transplantation	Autologous Transplantation
Leukemia (acute lymphoblastic, acute myelogenous, chronic myelogenous)	Effective	Controversial; no better than conventional therapy
Lymphomas (Hodgkin disease, non-Hodgkin lymphoma)	Effective	Used rarely and only when marrow not involved
Neuroblastoma (stage IV)	Controversial; studies ongoing to define role related to conventional therapy and autologous transplantation	Controversial; studies ongoing to define role related to conventional therapy and allogeneic transplantation
Bone and soft tissue sarcomas, Wilms tumor, brain tumors	Very rarely indicated	Rarely indicated and effectiveness unproven
Aplastic anemia and other cytopenias (not environmentally caused)	Effective	Not indicated
Immune deficiency (eg, severe combined immunodeficiency disease)	Effective	Not indicated
Hemoglobinopathies, thalassemia, sickle cell anemia	Effective	Not indicated
Metabolic storage disorders, Hurler syndrome, metachromatic leukodystrophy	Controversial; may be effective in selected patients	Not indicated

* See reference 3 in this article.

American Academy of Pediatrics (AAP) Statement on Cord Blood Banking

- Given the difficulty of making an accurate estimate of the need for autologous transplantation and the ready availability of allogeneic transplantation, private storage of cord blood as "biologic insurance" is unwise.
- Conditions such as leukemia or severe hemoglobinopathy may indicate the need for directed donor cord blood banking for sibling cord blood transplantation.

Stem cells from cord blood - current status and future potential

- 造血幹細胞移植 (HSCT)

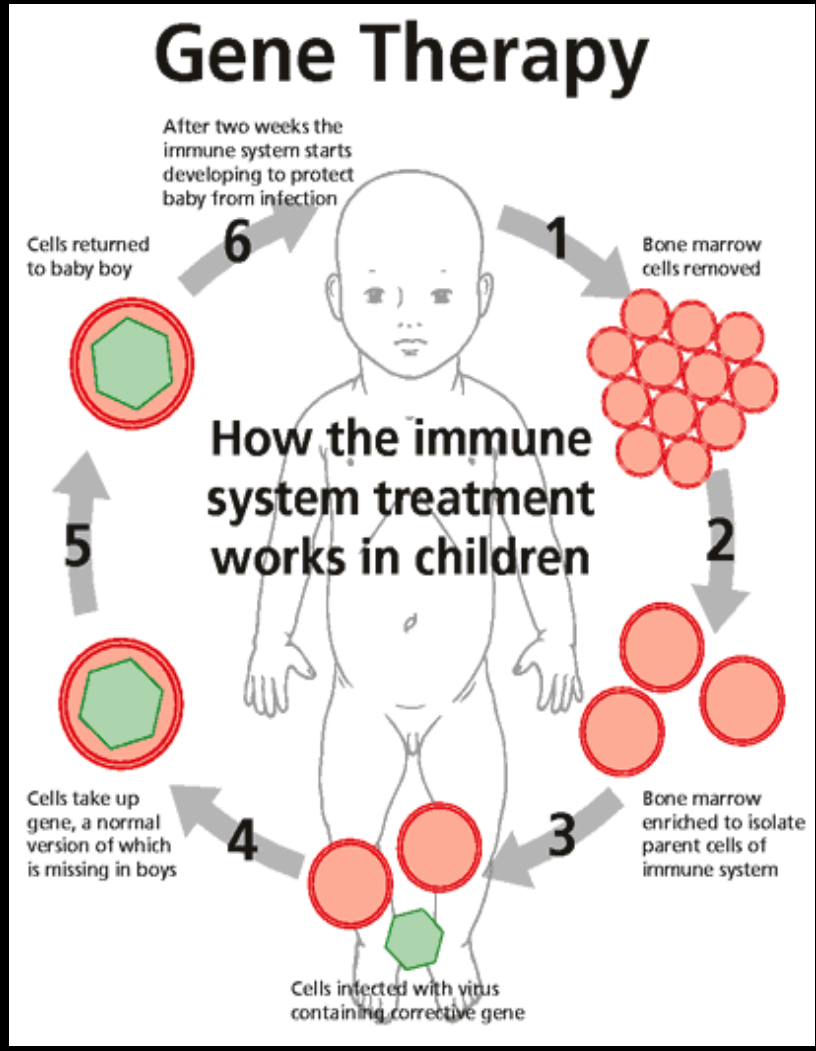
- **基因治療 (Gene therapy)**

- It is hoped that further research into gene therapy of human stem cells during development and differentiation may culminate in the successful correction of a defective gene in a human stem cell

- 再生醫學 (Regenerative Medicine)

Gene Therapy

- Autologous cord blood collections could be used as insurance against future illness requiring pluripotent stem cell support or as targets for gene therapy
- The genetically altered stem cells could then be infused into the patient



Gene Therapy

- The diseases caused by the defective genes can be treated and potentially cured by transfer of genetic material of specific cells of patient
- The success of gene therapy is dependent on the “efficiency” and “specificity” of the delivery system
- It’s recently been demonstrated that cord blood stem cells take up new genes more efficiently than bone marrow stem cells, making them an attractive vehicle for gene therapy

Gene Therapy

- The first attempt at gene therapy with cord blood in 1993 in three children suffering from adenosine deaminase (ADA) deficiency. The children, who also receive additional drug treatment, appear healthy to date, even though their blood now carries only a small amount of the gene introduced into their stem cells.

- Already, through gene therapy, cord blood cells have been used to cure children born with SCIDS, otherwise known as the “bubble boy” disease ***(Fagioli et al, 2003)***

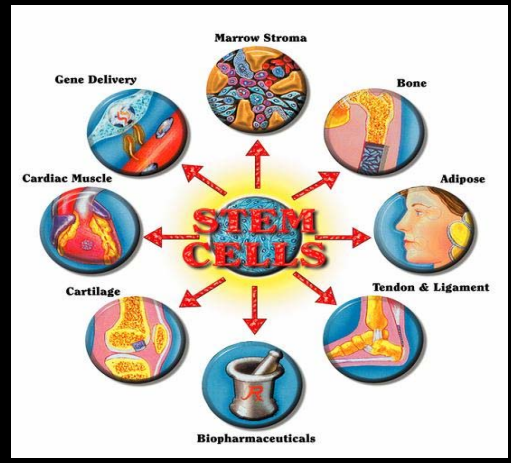
Anticipated Benefits of using Umbilical Cord Blood

- lower rate of graft vs. host disease
- higher transduction rates using retroviral vectors because cord blood has more stem cells in active cycle compared to adult bone marrow
- no more multiple sticks being inserted into the bone to obtain sufficient numbers of stem cells since cord blood is rich in stem cells
- no pain or harm to the baby or the mother when obtaining the blood
- reconstitution of the immune system
- discontinuation of the costly $250, 000/yr/patient PEG-ADA treatment

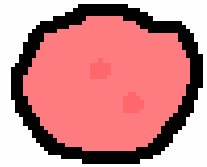
Stem cells from cord blood - current status and future potential

- 造血幹細胞移植 (HSCT)
- 基因治療 (Gene therapy)
- **再生醫學 (Regenerative Medicine)**

  Umbilical cord blood stem cells can apparently regenerate so much more than just the blood and immune systems

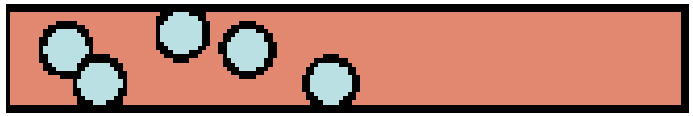


Blood Stem Cells

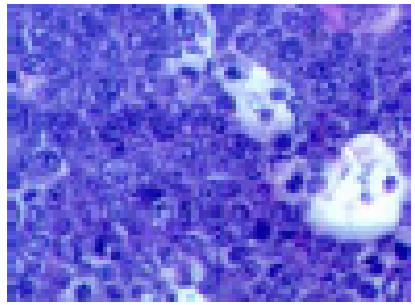


stem cell

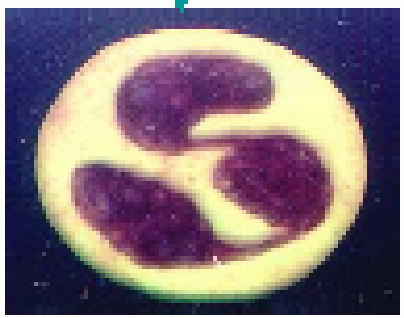
progenitor cell



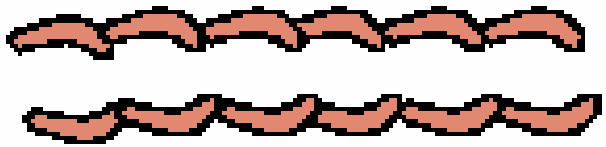
Vascular progenitor



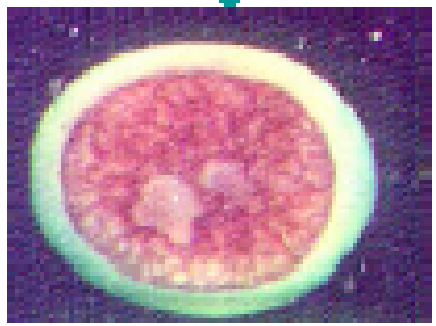
thymus cell



granulocyte

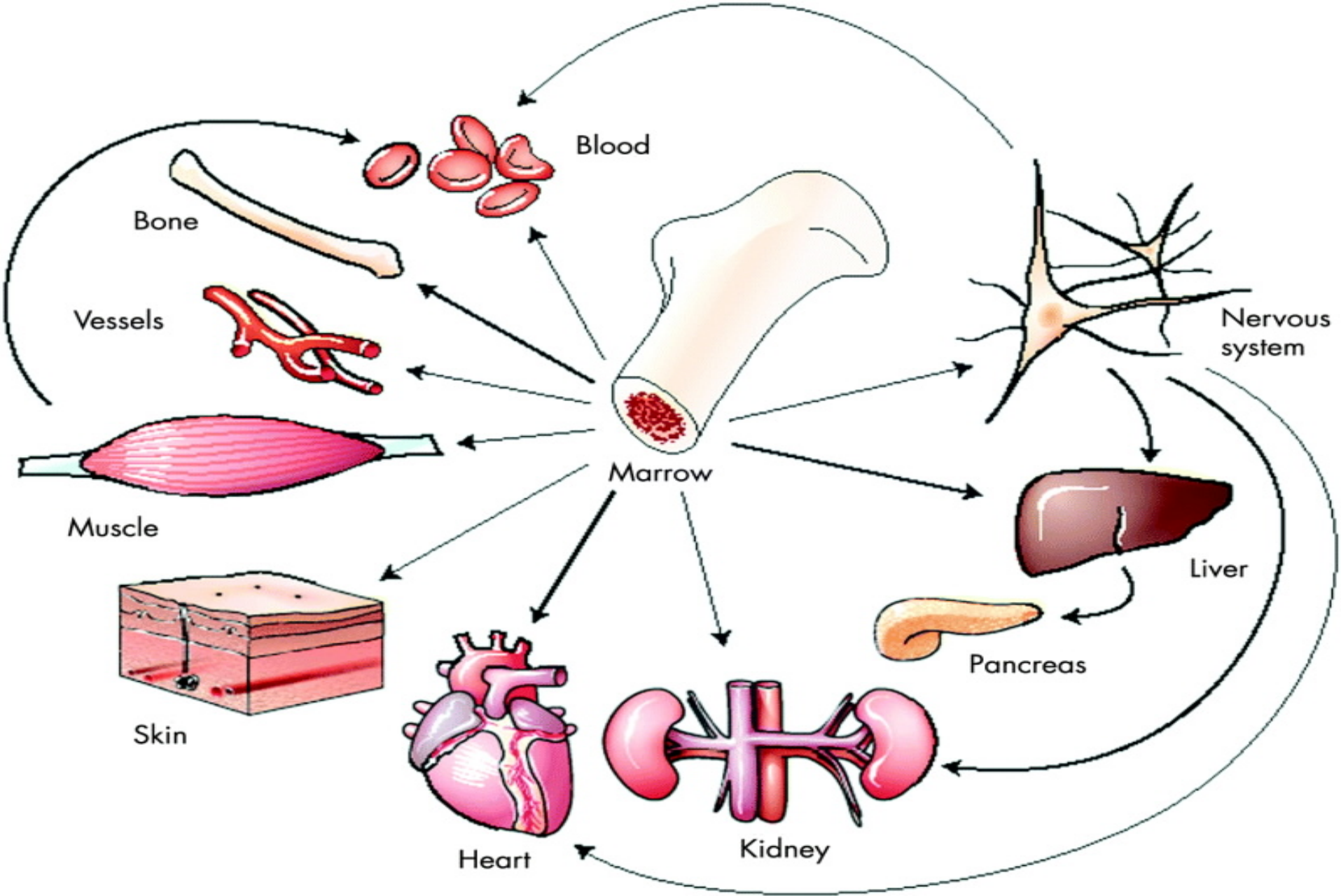


New blood vessel

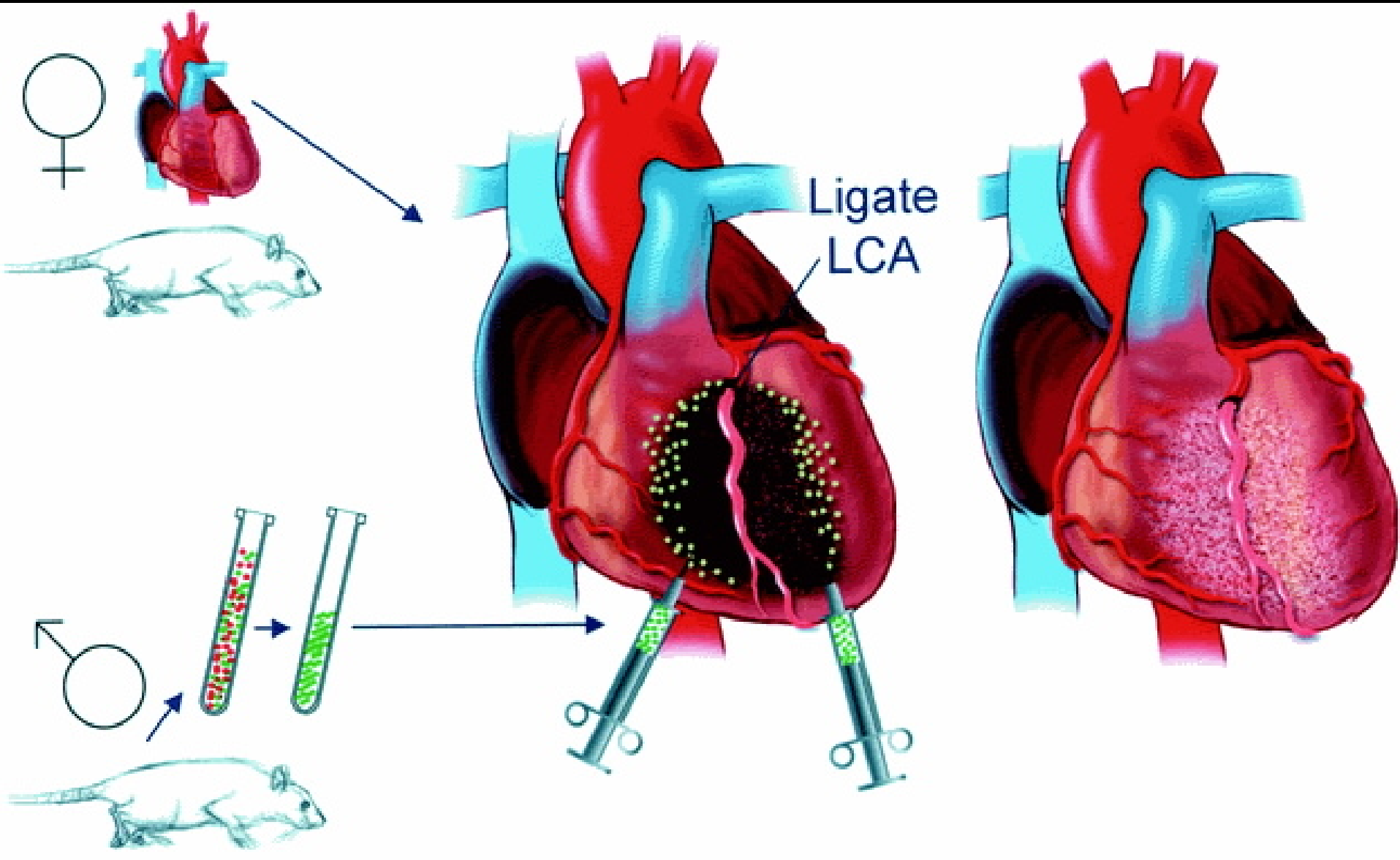


lymphocyte

Possible pathways of differentiation in adult stem cells



Myocardial Regeneration

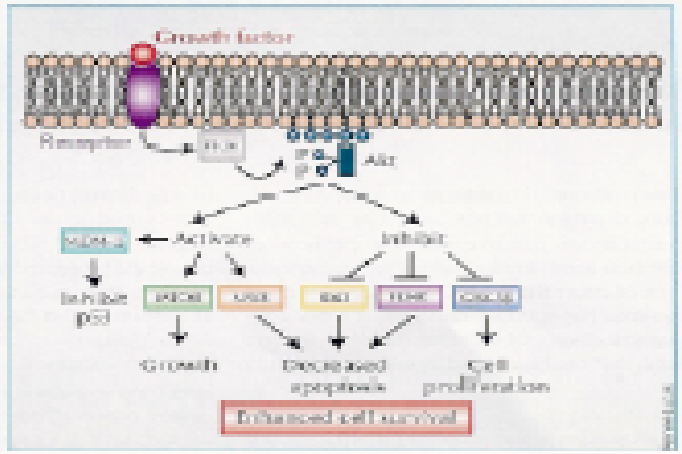


Clinical feasibility of intracoronary infusion of bone marrow cells for myocardial repair

MSC repair of the heart

Nature Medicine 9(9):1109, 2003

News and Views



Mesenchymal stem cells modified with Akt prevent remodeling and restore performance of infarcted hearts.

Mangi AA, Noiseux N, Kong D, He Huamei, Rezvani M, Ingwall JS, Dzau VJ
Brigham and Women's Hospital Harvard Medical School

Akt helps stem cells heal the heart

Koc ON, and Gerson SL

Nature Medicine 9(9):1109, 2003

Regenerative Medicine

- This is possible because cord blood, like bone marrow, contains regenerative stem cells that can replace diseased cells in an affected individual *(Ladewig 1998)*.
- Human UCB cells have many advantages as grafts for cell transplantation because of the immaturity of newborn cells compared with adult cells
- As a source of transplantable hepatic progenitor cells - a novel therapeutic option for liver failure *(Kakinuma et al, 2003)*

The European Group on Ethics in Science and New Technologies (歐洲研究倫理小組; EGE) Brussels, 18 March 2004

- The probability of needing an autologous transplantation has been estimated as approximately 1 in 20,000 during the first 20 years of life. Moreover, it has not yet been demonstrated that cells usable for transplantation can be stored for more than 15 years.
- No clear proof of the utility of stem cells has yet been shown and the possibility to use UCB for regenerative medicine is currently purely hypothetical

Stem cells from cord blood - current status and future potential

- the plasticity and multipotency of adult stem cells, which has been recently discovered, could lead to a possible **autologous use of cord blood stem cells** for different indications in the field of regenerative medicine (cell- and organ replacement / regeneration).
- So far, however, this remains speculative. Research in the field of stem cell development and differentiation in the next decade will try to find some answers