

III. わが国における臍帯血移植の動向

1. わが国における造血細胞移植の歴史

わが国において近代的骨髄移植が開始されたのは1970年代のことで、80年代にはHLA一致同胞間の骨髄移植が治療法として確立された。90年代前半から半ばにかけて新たな移植細胞源として末梢血幹細胞と臍帯血幹細胞が加わり、さらに90年代前半の骨髄バンク、後半の臍帯血バンク設立によりドナーが従来の同胞を中心とする血縁者から非血縁者まで拡大されてきた。

このような造血細胞移植の歴史と動向を、本研究班も関与しながら完成させた「造血細胞移植データ一元化事業」のデータなどによりまとめてみた。

2. 同種・自家（自己）別、血縁・非血縁別の造血細胞移植

日本における同種移植と自家移植の移植数の推移をみると、自家移植が90年代後半以降ほぼ一定の数で推移しているのに対し、同種移植はほぼ一定の比率で増加を続けているのが対照的である。（図1 上段）

また、同種移植を血縁者間移植と非血縁者間移植でみると、血縁者間移植が2000年代にプラトーに達しているのに対し、非血縁者間移植は1991年の骨髄バンクの設立、1999年の日本さい帯血バンクネットワークの設立などを契機として2000年代には着実に増加している。（図1 下段）

3. 血縁者間造血細胞移植

移植細胞源別に血縁者間造血幹細胞移植の推移をみると、小児では90年代後半から2000年代初頭に末梢血幹細胞移植が一旦増加傾向を示したものの、2000年代後半には減少していることがわかる。（図2 上段）

一方成人では、2000年に健康保険で末梢血幹細胞移植が認可されたことから2002年まで増加の一途をたどったが、その後は減少してこの数年は骨髄移植とほぼ同数で推移している。2000年代前半の末梢血幹細胞移植の増加の理由としては、幹細胞採取の利便性、移植後の生着の早さなどに加えて移植片対宿主病（GVHD）の増強による抗白血病効果への期待があった。しかし、この抗白血病効果は期待したほどなく、逆に慢性GVHDの増加によりQOLの低下が多くなったことから、再び骨髄移植が見直されたものである。（図2 下段）

4. 非血縁者間造血細胞移植

わが国における非血縁者間骨髄移植は1993年に開始され、2010年末までに12,500例ほど実施されている。一方非血縁者間臍帯血移植は1997年に開始され、2003年から急速に移植数が増加し、以後毎年骨髄移植とほぼ同数の移植が行われ、累積の移植数も7,000例を超えている。（図3）

非血縁者間造血幹細胞移植の実施数を細胞源にみると、小児では2000年より骨髄移植と臍帯血移植がほぼ同数で推移し、成人でも2003年以降ほぼ同数で増加傾向が続いている。（図4）

つぎに小児、成人の年齢層を細かく区切ってみると、小児では5歳未満の年齢層で臍帯血移植がより積極的に選択されており、成人では若年齢層で骨髄移植、高年齢層で臍帯血移植が選ばれている傾向がある。成人での移植数は50歳代から60歳代のいわゆる団塊の世代においてピークを形成しており、今後もこの年齢層を中心に移植数が増加するものと予想される。（図5）

5. 国際的な造血細胞移植の動向との比較

図6は国際造血幹細胞移植登録機構 (Center for International Blood and Marrow Transplant Research, CIBMTR) による同種造血幹細胞移植の移植細胞源別にみた統計で、左半分が20歳以下、右半分が20歳超の成人で、オレンジが骨髄移植、グリーンが末梢血幹細胞移植、ブルーが臍帯血移植を示している。また、それぞれ1999年から2003年の5年間と2004年から2008年までの5年間で比較している。

小児では前半、後半ともに骨髄移植がほぼ半数、残りの4分の1ずつを末梢血幹細胞移植と臍帯血移植が占めている。

一方、成人では末梢血幹細胞移植の割合が前半60%程度であったものが後半には80%と著明に増加しているのが特徴的である。

図7はわが国における同種造血幹細胞移植の実施状況をCIBMTRと同じように解析したのものであるが、小児では前半後半とも骨髄移植が60%、臍帯血移植が40%弱であり、成人では前半では骨髄移植、末梢血幹細胞移植、臍帯血移植が3:2:1の割合であったものが、後半には骨髄移植がほぼ半数、臍帯血移植が末梢血幹細胞移植をやや上回って増加しているのが、欧米との顕著な差となっている。

非血縁者間造血幹細胞移植を見てみると日本と欧米との差はさらに顕著である。

欧米においては小児において臍帯血移植の実施数が増加しているのに対し、成人では末梢血幹細胞移植が飛躍的に増加している。(図8)

一方、わが国では小児成人とも末梢血幹細胞移植はほぼゼロである点が欧米と大きく異なるが、これはわが国の骨髄バンクではこれまで末梢血幹細胞移植が行われていなかったことによるものである。小児、成人のいずれにおいても後半の時期には骨髄移植と臍帯血移植がほぼ同数となっており、特に成人における臍帯血移植の増加はわが国に特徴的な現象といえる。(図9)

6. わが国の各臍帯血バンクの臍帯血公開数

図10にわが国の臍帯血公開数を臍帯血バンク毎に暦年別に示した。日本臍帯血バンクネットワークでは保存可能臍帯血の有核細胞数下限を発足当時の 3×10^8 個から 6×10^8 個、 8×10^8 個と変更しながら、より多い細胞数を含む臍帯血を保存してきた。その結果、年毎の保存件数や公開件数は減少しているものの、移植に提供される臍帯血の本数は年々増加し、最近では京阪さい帯血バンクの提供件数の伸びが顕著である。(図11)

7. 国際的な臍帯血バンクの活動状況

世界骨髄バンク連合 (World Marrow Donor Association, WMDA) には世界の主な骨髄バンクや臍帯血バンクが加盟し、非血縁者間造血細胞移植 (骨髄、末梢血幹細胞、臍帯血) に関するデータを収集し、その統計を公表している。

2009年にはWMDAに加盟する139の臍帯血バンクから3,792の臍帯血が提供されており、この中にはわが国の893の臍帯血が含まれている。欧米では成人の臍帯血移植の多くが複数臍帯血移植で行われ、わが国ではほとんどが単数臍帯血移植であることから、移植数でみた場合世界の非血縁者間臍帯血移植の約3分の1を日本が占めていることになる。

図1. 日本における造血細胞移植1980-2008
(1) 同種・自家、血縁・非血縁

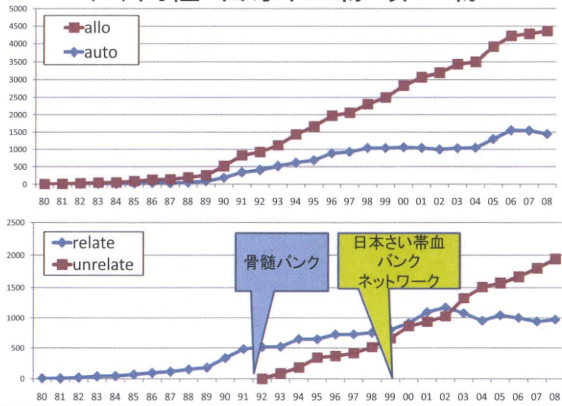


図2. 日本における造血細胞移植1980-2008
(2) 血縁者間移植における細胞源

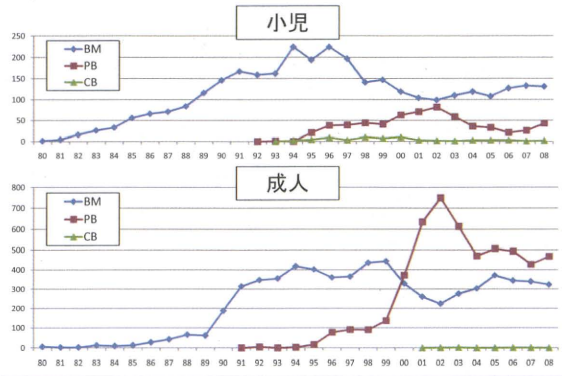


図3. (3) 非血縁者間造血細胞移植
1993-2010

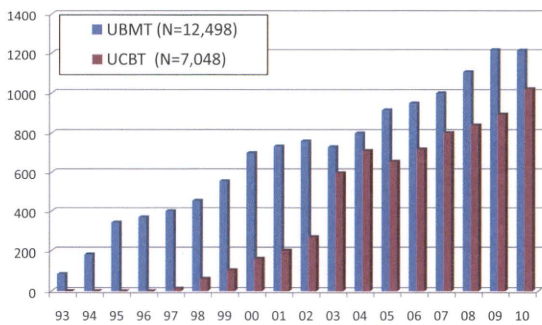


図4. 日本における造血細胞移植1980-2008
(4) 非血縁者間移植における細胞源

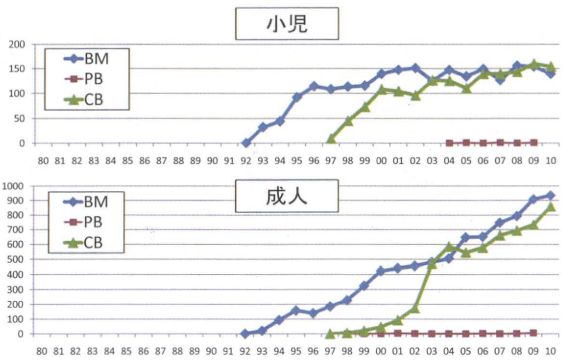


図5. (5) 非血縁者間造血細胞移植
年齢層別推移
1993-2010

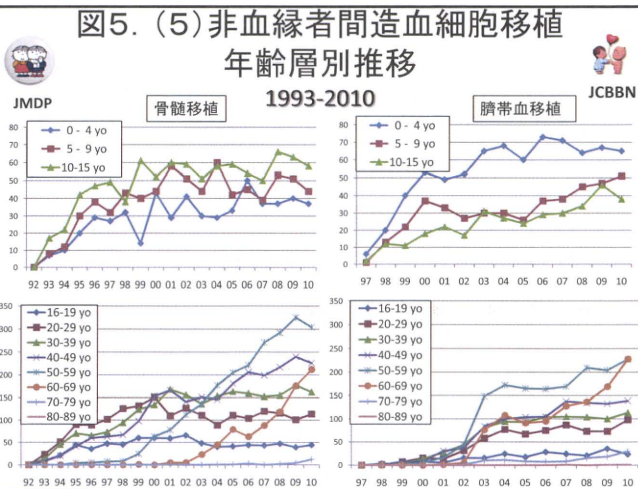


図6. Allogeneic stem cell sources,
by recipient age
1999-2008

CIBMTR

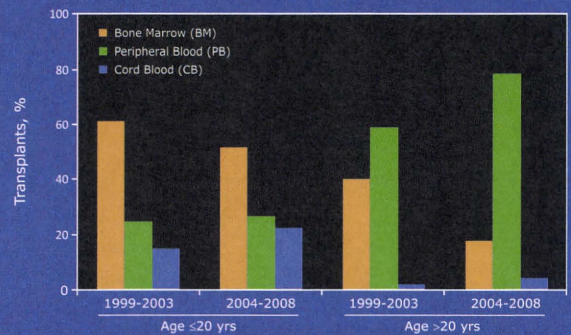


図7. Allogeneic stem cell sources, by recipient age in Japan 1999-2008

JSHCT

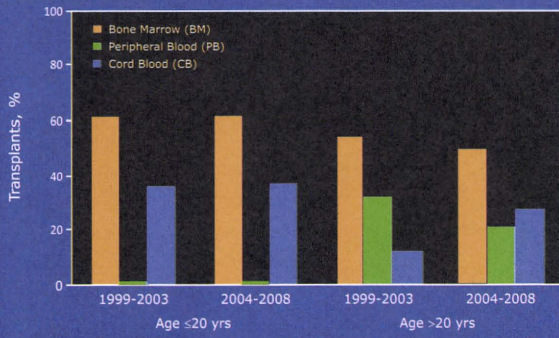


図8. Unrelated donor stem cell sources by recipient age 1999-2008

CIBMTR

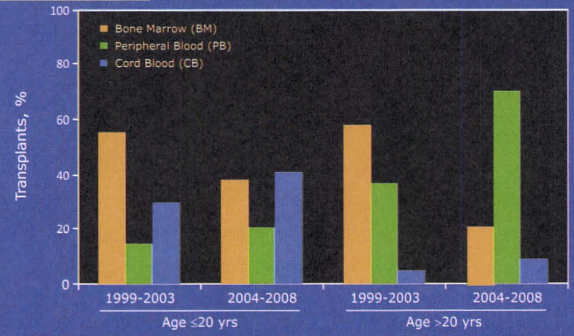


図9. Unrelated donor stem cell sources by recipient age in Japan 1999-2008

JSHCT

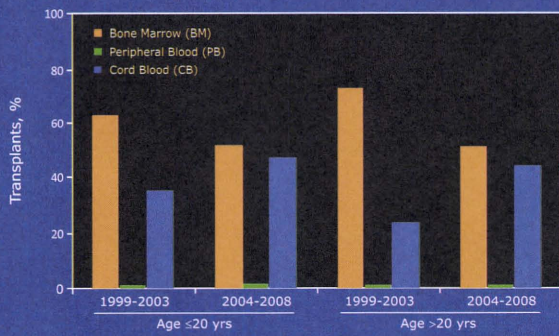


図10. 各臍帯血バンクの公開数* (暦年別推移: *保存数ではない)

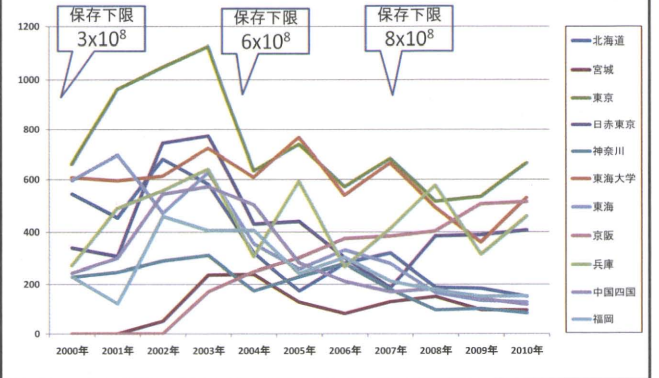


図11. 各臍帯血バンクの提供数 (暦年別推移: 複数臍帯血移植を含む)

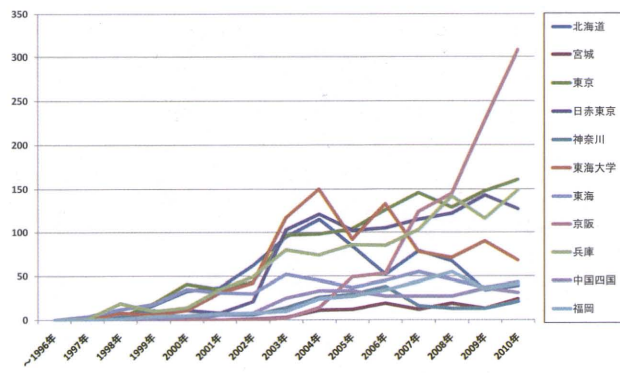
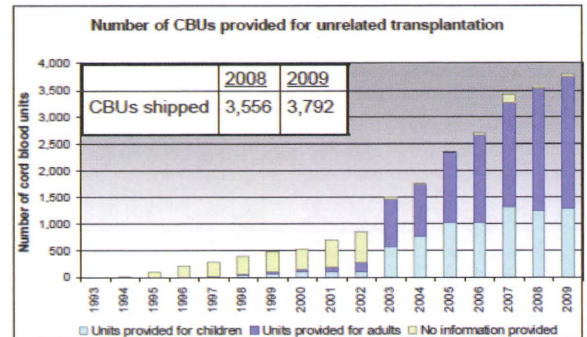


図12. 世界の臍帯血提供数
In 2009, 139 Cord Blood Banks worldwide participated



IV. 研究成果の刊行に関する一覧表

加藤 俊一

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東 英一

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