# Hematopoietic Stem Cell Transplantation
# Differences in Inherited Bone Marrow Failure Syndromes (IBMFS)
# vs.
# Acquired Aplastic Anemia (AA)

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# Overview

- HSCT is a curative treatment for both IBMFS and AA.
- IBMFS: Genetic disorders with multi-organ involvement and cancer predisposition.
- AA: Immune-mediated bone marrow failure, often idiopathic or triggered by environmental factors.
- Differences in etiology, indications, donor selection, conditioning, outcomes, and post-transplant management.

# Key Differences in Indications for HSCT:

| Aspect | IBMFS | Acquired AA |
|---|---|---|
| **Primary Indication** | Severe bone marrow failure or progression to MDS/AML. | Severe or very severe AA, particularly in younger patients. |
| **Refractory Disease** | HSCT is often the only curative option for refractory cytopenias. | HSCT is indicated for patients refractory to IST. |
| **Clonal Evolution** | High risk of MDS/AML; HSCT is often performed preemptively. | HSCT is indicated for clonal evolution (e.g., PNH, MDS, AML). |
| **Age Considerations** | Timing of HSCT depends on syndrome-specific risks and disease severity. | HSCT is preferred in younger patients; IST is first-line in older patients. |
| **Donor Availability** | Matched sibling donors are preferred, but alternative donors may be used. | Matched sibling donors are preferred; alternative donors considered if unavailable |

# FA & Clonal evolution

- Gain of chromosome 1q is the most common abnormality in FA; it can occur without MDS/AML and does not necessarily indicate impending transformation.
- Conversely, monosomy 7/del(7q) is considered a marker of transformation, requiring urgent HSCT.
- Other cytogenetic changes indicating a poor prognosis are gain of chromosome 3q, frequently preceding monosomy 7/del(7q),21,22 and RUNX1 abnormalities, including cryptic translocations, that also indicate immediate HSCT.
- Special attention is warranted for BRCA2 patients, who, due to the extremely high occurrence of AML (cumulative incidence [CI] of 80%) and solid cancers (CI of 97%) within the first 10 years of age, may be considered for preemptive HSCT.

# Key Differences in Donor Selection and Conditioning:

| Aspect | IBMFS | Acquired AA |
|---|---|---|
| **Donor Preference** | Matched sibling donor (with genetic screening); alternative donors used if unavailable. | Matched sibling donor preferred; unrelated or haploidentical donors considered. |
| **Conditioning Intensity** | Reduced-intensity or non-myeloablative due to DNA repair defects and toxicity risks. | Reduced-intensity preferred; myeloablative used selectively in younger patients. |
| **Toxicity Concerns** | High sensitivity to alkylators and radiation; syndrome-specific adjustments required.( DKC, FA ) | Toxicity concerns are lower but still significant in older patients. |
| **GVHD Risk** | Higher risk due to genetic predisposition and multi-organ involvement. | GVHD risk is moderate; manageable with standard prophylaxis. |

# Donor Selection and Conditioning Regimens – Inherited Bone Marrow Failure Syndromes (IBMFS):

- **Special Considerations:**
- Pre-Transplant Evaluation: Patients with IBMFS often require extensive pre-transplant evaluations to assess organ function (e.g., cardiac, pulmonary, hepatic) due to the multi-system nature of these disorders.

# Donor Selection and Conditioning Regimens – Inherited Bone Marrow Failure Syndromes (IBMFS):

- **Special Considerations:**
- **Avoidance of FA Carriers:**
  - Primary concern is the recipient's condition rather than the donor's carrier status.
  - The decision to avoid FA carriers in HSCT is primarily driven by the need to minimize transplant-related complications and improve outcomes for patients with FA.
  - FA carriers, while not affected by the disease, may still present risks if used as donors due to potential genetic implications. The focus is often on finding non-carrier donors to ensure the best possible outcomes for the recipient.
  - **While avoiding FA carriers in HSCT is a prudent approach to minimize risks, it is essential to balance this with the availability of suitable donors**

# Donor Selection and Conditioning Regimens – Acquired Aplastic Anemia (AA):

- **Special Considerations:**
- Age and Comorbidities: Younger patients (<40 years) generally tolerate HSCT better and have superior outcomes. Older patients or those with comorbidities may require tailored RIC regimens.

- Prior Immunosuppressive Therapy (IST): Patients who have failed IST (e.g., ATG + cyclosporine) may have a higher risk of graft rejection, necessitating more intensive conditioning.

# Key Differences in Outcomes and Complications:



| Aspect | IBMFS | Acquired AA |
|---|---|---|
| **Survival Rates** | Variable (50-90%) depending on syndrome and donor type. | Generally excellent (80-90% with MSD, 70-80% with MUD). |
| **GVHD Risk** | Higher due to genetic predisposition and multi-organ involvement. | Moderate; manageable with prophylaxis |
| **Organ Toxicity** | High due to underlying DNA repair defects and sensitivity to conditioning. ( FA & mucositis, DKC & BOOP, VOD ) | Lower but still significant, particularly in older patients. |
| **Infections** | Higher risk due to delayed immune reconstitution and prolonged immunosuppression. | Significant risk, particularly in the early post-transplant period. |
| **Secondary Malignancies** | High risk, particularly in Fanconi anemia and dyskeratosis congenita. | Lower risk but still a concern, especially with TBI or alkylators. |
| **Long-Term Monitoring** | Lifelong monitoring for syndrome-specific complications and malignancies. | Regular monitoring for chronic GVHD, infections, and late effects. |

# Key Differences in Post-Transplant Management:

| Aspect | IBMFS | Acquired AA |
|---|---|---|
| **Immune Reconstitution** | Delayed due to underlying genetic defects and reduced-intensity conditioning. | Generally faster but can be delayed in older patients or with chronic GVHD. |
| **Infection Prophylaxis** | High risk of infections due to prolonged immunosuppression and delayed recovery. | Significant risk, particularly in the early post-transplant period. |
| **GVHD Management** | Higher risk of chronic GVHD; requires long-term immunosuppression. | Moderate risk; manageable with prophylaxis and supportive care. |
| **Syndrome-Specific Monitoring** | Lifelong monitoring for syndrome-specific complications and malignancies. ( FA & SCC, DKC & PF ) | Regular monitoring for chronic GVHD, infections, and late effects. |
| **Secondary Malignancies** | High risk, particularly in Fanconi anemia and dyskeratosis congenita. | Lower risk but still a concern, especially with TBI or alkylators. |
| **Psychosocial Support** | Essential due to chronic nature of IBMFS and impact on quality of life. | Important for managing long-term effects of HSCT on quality of life. |

# Key Differences Summary

- **Key Points:**
- **Etiology:** Genetic (IBMFS) vs. immune-mediated (AA).
- **Indications:** Severe cytopenias, MDS/AML (IBMFS) vs. severe AA, refractory to IST (AA).
- **Donor Selection:** Genetic screening in IBMFS; matched sibling preferred in both.
- **Conditioning:** Reduced-intensity in IBMFS; reduced-intensity or myeloablative in AA.
- **Outcomes**: Higher complications in IBMFS; better survival in AA.
- **Post-Transplant:** Lifelong monitoring in IBMFS; focus on GVHD and infections in AA.