and diabetes mellitus. To prevent these symptoms, patients who develop marked elevations in transferrin saturation or serum ferritin levels should undergo iron chelation therapy with deferoxamine or an oral agent (e.g., deferiprone).

Chronic administration of recombinant EPO reduces the transfusion needs of some MDS patients, particularly those with low endogenous serum EPO levels and few transfusion requirements. Individuals with recurrent or refractory neutropenic infections often receive G-CSF and GM-CSF treatment alone or in addition to EPO and antibiotic regimens. These treatments are supportive and do not affect overall survival.

TABLE 45-5 WORLD HEALTH ORGANIZATION CLASSIFICATION OF MYELODYSPLASTIC SYNDROMES

CLASS	DEFINITION
Refractory anemia	Blood: anemia, no or rare blasts BM: erythroid dysplasia only, <5% blasts, and <15% ringed sideroblasts
Refractory anemia with ringed sideroblasts (RARS)	Blood: anemia, no blasts BM: ≥15% ringed sideroblasts, erythroid dysplasia only, <5% blasts
Refractory cytopenia with multilineage dysplasia (RCMD)	Blood: cytopenias (bicytopenia or pancytopenia), no or rare blasts, $<1 \times 10^9$/L monocytes BM: dysplasia in ≥10% of the cells of two or more myeloid cell lines, <5% blasts, no Auer rods, <15% ringed sideroblasts
Refractory cytopenia with multilineage dysplasia and ringed sideroblasts (RCMD-RS)	Blood: cytopenias (two or more), no or rare blasts, no Auer rods, and $<1 \times 10^9$/L monocytes BM: dysplasia in ≥10% of the cells of two or more myeloid cell lines, <5% blasts, ≥15% ringed sideroblasts, no Auer rods
Refractory anemia with excess blasts type 1 (RAEB-1)	Blood: cytopenias, <5% blasts, no Auer rods, $<1 \times 10^9$/L monocytes BM: unilineage or multilineage dysplasia, 5-9% blasts, no Auer rods
Refractory anemia with excess blasts type 2 (RAEB-2)	Blood: cytopenias, 5-19% blasts, Auer rods ± $<1 \times 10^9$/L monocytes BM: unilineage or multilineage dysplasia, 10-19% blasts, ± Auer rods
Myelodysplastic syndrome–unclassified (MDS-U)	Blood: cytopenias, no or rare blasts, no Auer rods BM: unilineage dysplasia in one myeloid line, <5% blasts, no Auer rods
MDS associated with isolated del(5q)	Blood: anemia, usually normal or increased platelet count, <5% blasts BM: normal to increased megakaryocytes with hypolobulated nuclei, <5% blasts, isolated cytogenetic abnormality of deletion 5q, no Auer rods

BM, Bone marrow.

Immunosuppressive Therapy

Certain MDS disease subgroups appear to have hematopoietic failure mediated in part by autoimmune cells selectively targeting the destruction of normal HSCs. These disease subsets exhibit significant overlap with AA and PNH. For instance, some young patients with low-risk MDS disease and an HLA-DR15 haplotype have demonstrated a 30% to 50% improvement in counts after T-cell immunosuppressive therapy with ATG or cyclosporine. MDS patients with isolated trisomy 8 or demonstrated PNH clones, or both, have responded to treatment with immunosuppressive agents.

Stem Cell Transplantation

As in other hematologic stem cell disorders, the only curative therapy for MDS patients remains allogeneic stem cell transplantation, ideally performed at complete remission. All MDS patients younger than 40 years with an available HLA-matched sibling donor should be offered transplantation at diagnosis. Long-term, disease-free survival rates for patients with low-risk disease are greater than 50%. However, the high transplantation-related mortality, morbidity, and relapse rates associated with mismatched or unrelated donor transplants or with transplantation in older MDS patients have limited the use of these forms of transplantation to patients with high-risk disease.

Patients with intermediate-2 or high-risk MDS (i.e., MDS with cytogenetic abnormalities predisposing to leukemic transformation or high levels of circulating blasts with International Prognostic Scoring System [IPSS] scores of intermediate-2 or higher) (Table 45-6) may be offered acute leukemia-based chemotherapy regimens (see Chapter 46) designed to eradicate rapidly proliferating blast cells, not dysfunctional MDS cells. These therapies for MDS patients are associated with a high relapse rate within 12 to 18 months and no significant prolongation of overall survival, even for patients who achieve remission.

Targeted Therapeutic Agents

Although not curative, a panoply of novel therapeutic agents targeting the unique biologic features of MDS have improved outcomes for many MDS patients ineligible for or unwilling to pursue stem cell transplantation or supportive care. Administered largely in the outpatient setting, these agents have induced disease remissions, retarded leukemia evolution, and for the first time, prolonged overall survival of MDS patients.

TABLE 45-6 WORLD HEALTH ORGANIZATION CLASSIFICATION-BASED PROGNOSTIC SCORING SYSTEM (WPSS) FOR MYELODYSPLASTIC DISORDERS

	*SCORING**			
FACTOR	***0***	***1***	***2***	***3***
WHO category	RA, RARS, 5q–	RCMD, RCMD-RS	RAEB-1	RAEB-2
Karyotype†	Good	Intermediate	Poor	—
Transfusion requirement‡	No	Regular	—	—

MDS, Myelodysplastic syndrome; RA, refractory anemia; RARS, refractory anemia with ringed sideroblasts; RCMD, refractory cytopenia with multilineage dysplasia; RCMD-RS, refractory cytopenia with multilineage dysplasia and ringed sideroblasts; RAEB-1, refractory anemia with excess of blasts type 1; RAEB-2, refractory anemia with excess of blasts type 2; 5q–, myelodysplastic syndrome with isolated del(5q) and marrow blasts less than 5%; WHO, World Health Organization.

*Risk groups were determined as follows: very low (total score = 0), low (1), intermediate (2), high (3 to 4), and very high (5 to 6).

†Karyotype was as follows: good: normal, –Y, del(5q), del(20q); poor: complex (≥3 abnormalities), chromosome 7 anomalies; and intermediate: other abnormalities.

‡Red blood cell (RBC) transfusion dependency was defined as having at least one RBC transfusion every 8 weeks over a period of 4 months.