WHERE’S THE %#@*&^ TICK BOX?

Conditions Affecting Outcomes
- Disease and remission status
- Recipient age
- Donor-recipient compatibility
- Performance status
- Co-morbid conditions
  - Cardiac, respiratory, hepatic and renal
- Previous infections
- Nutritional status

Baseline Forms
- Captures essential pre-transplant data
  - Patient
  - Comorbid diseases
  - Conditioning
  - Graft
  - Donor
Disease Information

- Critical to determine purpose of HCT, outcomes, adjustment for disease status pre-transplant
- WHO updates
- Look carefully for the disease whenever considering the “900” box
  - 1-900-Check Again

Conditioning Regimens

- Everyone gets one (almost)
- Record the actual drugs, not the acronym
  - BEAM =
    - Carmustine
    - Etoposide
    - Cytarabine
    - Melphalan

Co-Existing Diseases

- Outcomes of transplant depend upon more than the disease for which HCT done
- Co-existing diseases complicate HCT (Sorror et al, Blood; 2005)
- Look carefully for the co-existing disease
Co-Existing Examples

- Don’t just record the whole Past Medical History
  - High blood pressure = HTN
  - Stroke=CVA
  - Vasectomy = Who cares?
- Don’t report unless a category exists OR truly significant to the HCT

Cardiac

Risk factors for cardiac dysfunction
- Recipient age > 50 years
- Prior exposure
  - Anthracycline
  - Cyclophosphamide
- CAD, CCF, hypertension, cardiomyopathy

Report Form

- Coronary artery disease
- Hypertension
- Other
  - Total dose (mg/m² or mg/kg) of anthracycline and/or cyclophosphamide
  - Congestive cardiac failure
  - Cardiomyopathy
  - Ejection fraction/MUGA
Common Mistakes

- Cardiac
  - Palpitations
  - Hypotension
- If reporting results of MUGA/ECHO:
  - attach results or report as indicated in the Report
- Please do not report the following:
  - Ejection murmur
  - Heart murmur
  - Heart surgery

Blood/Report Form

- Deep vein thrombosis
- Hemophilia
- Drugs
  - Anticoagulants
  - Factor replacement
- Central nervous system bleed
- Refractory to PRBC/platelet transfusion

Common Mistakes

- Bleeding
  - Epistaxis
  - Menorrhagia
- Anemia
Respiratory

- Pulmonary function tests
  - Diffusion capacity
  - Forced expiratory volume
  - Forced vital capacity
- Prior history
  - Asthma, cystic fibrosis, bronchiectasis, COPD, pulmonary embolism, ARDS

Report Form

- Asthma
- Other
  - Cystic fibrosis, bronchiectasis
  - COPD
  - Pulmonary embolism
  - Mechanical ventilation
  - Smoking

Report Form

- Smoking history
  - Establish whether HCT recipient is a smoker
  - Active smoker?
  - Average number of packs/day
  - Number of years: smoked
  - History of bronchitis
Common Mistakes

- Prior history of (if not related to a fungal infection):
  - Pleural effusion
  - Pneumonia
  - Pneumothorax
  - Seasonal allergies
  - Allergic rhinitis

Hepatic

- Liver function tests
  - ALT, AST, bilirubin
- Hepatitis
  - A, B, C, non-A, B, C
- VOD
  - Prior abdominal radiation
  - Acyclovir
  - Actinomycin-D

Report Form

- Drug toxicity
  - ALT and AST
- Viral infection
  - Hepatitis A, B, C
- Other
  - VOD
  - Iron overload
  - Congenital liver disorders
Gastrointestinal/Report Form

- Inflammatory bowel disease
  - Crohn’s disease
  - Ulcerative colitis
- Peptic ulcer disease
- Dysmotility
- Non-infectious hepatitis
- History of abdominal surgery

Renal/Report Form

- Creatinine
  - History of nephrectomy
  - Glomerulonephritis
  - Abdominal radiation
  - Proteinuria
  - Electrolyte wasting (renal fanconi)
  - Dialysis

Common Mistakes

- Prostatic hyperplasia
- Hemorrhagic cystitis
- Urinary tract infection
- Tubal ligation
- Vasectomy
- Ectopic pregnancy
Endocrine/Report Form

- Diabetes mellitus
- Thyroid disease
- Other
  - Adrenal insufficiency
  - Hypopituitarism
  - Hypo/hyper-parathyroidism
- Chronic steroid therapy
- Hyperlipidemia

Common Mistakes

- Diabetes mellitus is a comorbid condition if patient is receiving treatment
- Gestational diabetes should not be listed as a comorbid condition
- Electrolyte abnormalities like low/high K+

Fungal Infections

- Invasive fungal infection
  - Aspergillus
  - Candida
- Site
- Interval between infection and HCT
- Number of documented infections
Viral Infections

- Serological evidence
  - CMV
  - EBV
  - Hepatitis A, B, C
  - HTLV1
  - HIV

Congenital

- Chromosomal
  - Down’s syndrome
  - Bloom
- Fanconi anemia
- PNH
- Kostmann agranulocytosis
- Li-Fraumeni syndrome

Malignancy

- Any history of prior malignancy is important
- Is the current indication for HCT related to prior malignancy e.g. therapy related leukemia?
CNS/Psychiatric/Report Form

- Seizure disorder
- Depression
- Anxiety
- Schizophrenia
- Personality disorder
- Medications
  - May interact with transplant-related medications

Common Mistakes

- Non specific symptoms
  - Headaches
  - Blurred vision
- Carpal tunnel syndrome
- Chronic fatigue ?? Depression
- Gun shot wounds
- Migraine

Common Mistakes

- Other examples
  - Tonsillitis
  - Appendectomy
  - Cholecystectomy
  - Benign polyps
  - Hemorrhoids
  - Diverticulitis
  - Heart burn
  - Irritable bowel syndrome
Day 100 Form

- Captures essential post-transplant data
  - Hematopoietic recovery
  - Graft-versus-host disease
  - Infections
  - Organ complications relevant to HCT
    - Lung: occurs in 40-60% of HCT recipients
    - Liver
    - Other organs: endocrine, cardiac, renal

Pulmonary Complications

- Early (<30 days)
  - Infections (bacteria, fungi, viruses, aspiration)
  - Non-infectious (cardiac dysfunction, hypervolemia, capillary-leak syndrome, VOD)
- Middle (30 – 100 days)
  - CMV, HHV6, PCP, fungi, IPN, DAH
- Late (>100 days)
  - Infections (bacteria, fungi, viruses, PCP, Nocardia, mycobacterium)
  - Obstructive airway disease, bronchiolitis obliterans

Non-infectious Pulmonary Complications

- Interstitial pneumonitis (IPN)
- Idiopathic pneumonia syndrome (IPS)
- Diffuse alveolar hemorrhage (DAH)
- Bronchiolitis obliterans (BO)
- Engraftment syndrome (ES)
- Pleural effusion
- Pulmonary vascular disease
Diagnostic Tests

- Chest X-ray (helpful but not diagnostic)
- BAL usually the procedure of choice
- Trans-bronchial biopsy
- CT guided biopsy
- Video assisted thoracoscopy (VAT) and biopsy
- Open lung biopsy

Interstitial Pneumonitis

- Typically occur within 100 days after HCT but can occur later
- Widespread alveolar damage
  - Clinical manifestations
    - Cough, tachypnea, dyspnea, crackles, wheezing, hypoxemia
  - Bilateral infiltrates on chest x-ray and CT scan
  - May require mechanical ventilation

Interstitial Pneumonitis

- Postulated etiologies
  - Viral infections
  - Occult infection
  - Regimen-related toxicity
  - Cell-mediated immunity
  - Cytokine mediators
    - TNF, IL-8
  - Advanced IPN can progress to pulmonary fibrosis
Interstitial Pneumonitis

- Report Form
  - Bacterial or fungal infection should be reported under section on “Infections”
  - Date of onset of IPN
  - Diagnostic tests performed
  - Infection
    - Non-bacterial, Non-fungal
    - Will allow reporting of IPN if BAL/biopsy (+) for virus

Idiopathic Pneumonia Syndrome

- Similar to viral induced IPN except
  - Diagnosis of exclusion
    - BAL must be negative for bacterial/fungal/viral agents
  - Etiology
    - Occult infection, RRT, cell-mediated immunity

Diffuse Alveolar Hemorrhage

- Diffuse pulmonary infiltrates
- Cough, dyspnea, crackles, hypoxia
- Classic finding on BAL
  - Bloody return; RBCs; hemosiderin-laden macrophages; culture negative
- Etiology: occult infection, RRT, immunological abnormalities related to engraftment
**Bronchiolitis Obliterans**

- Obstructive airway
- Gradual onset dyspnea
- Occurs 3-12 months after HCT
- Wheezing that does not respond to bronchodilator therapy
- ↓DLCO
- CT scan: bronchial dilatation and air trapping on expiration
- Often, tissue biopsy is not required

**Engraftment Syndrome**

- Pulmonary infiltrates occurring with neutrophil recovery
- Chest X-ray/Chest CT scan
  - Multiple infiltrates
- Diagnostic tests such as BAL, biopsy must be negative for bacterial/fungal/viral infections

**Pleural Disease**

- Pleural effusion
  - Common
  - Often related to fluid overload
  - Other causes
    - VOD, RRT, infection
    - Though rare can occur with GVHD
    - Pleural effusion as an “other specify” is meaningless as the effusion is a consequence of one of the conditions listed above
Pulmonary Vascular Disease

- Though there are reports of the following these are very rare
  - Pulmonary VOD
  - Pulmonary venous thromboembolism
- If present should be reported under the “other specify” category

Common Mistakes

- “Other” category: question
  - A-V malformation (not a complication of HCT)
  - Capillary leak syndrome
  - Infiltrates (non-specific)
  - Bronchiectasis (infection)
  - Pneumothorax (non-specific)
  - Pulmonary nodules (non-specific)
    - If disease-related: Disease-specific insert
  - Pulmonary edema (non-specific)
  - Atelectasis

Hepatic Complications

- Veno-occlusive disease (VOD)
- Liver cirrhosis
- Viral infections
  - Hepatitis, CMV, adeno, HSV, HHV-6 and -8
  - Cholestatis (2nd to CSA and FK506)
- Bacterial infection resulting in cholestasis or fungal infection should be reported under “infections”
Diagnosis of Hepatic Complications

- Presence of jaundice (total bilirubin > 4 mg/dl)
- Elevated transaminases (viral infections, drugs)
- Radiological tests
  - Liver ultrasound with doppler
  - CT or MRI imaging
- Liver biopsy

Veno-occlusive Disease

- Most frequent of the complications affecting the liver
- Risk factors
  - Busulfan based regimen
  - Cy based regimen
  - TBI >1320 cGy
  - Prior abdominal radiation
  - Prior hepatitis C infection
  - Underlying liver inflammation or fibrosis

Veno-occlusive Disease

- What is VOD?
  - Injury to the sinusoids of the liver
  - Sinusoids are lined by endothelial cells which are damaged
  - Damaged cells then obstruct sinusoidal blood flow
  - Parenchymal damage is a late event
Veno-occlusive Disease

- Clinical features
  - Weight gain, Jaundice, Tender and enlarged liver
- Laboratory features
  - ↑Total bilirubin, ↑Transaminases
- Radiological
  - Slow/reversed portal vein flow, high congestion index, portal vein thrombosis, ↑resistive index to hepatic artery flow

Liver biopsy and direct measurement of hepatic venous pressure is rarely required for the diagnosis

Conditions that mimic VOD
- Sepsis
- Cholestatic liver disease
- Hemolysis
- Congestive heart failure
- Hyperacute GVHD
Liver Cirrhosis

- Late complication
- Occurs several years after HCT
- Hepatitis C viral infection is the predominant cause of cirrhosis
- Others: Hepatitis B, CAH, Iron overload
- Diagnosis: liver biopsy
- Candidates for liver transplantation

Common Mistakes

- “Other” category: question
  - Bacterial or fungal infections
  - GVHD
  - Fatty liver, List of drugs
  - Gilbert’s disease
  - ABO incompatibility
  - Chemotherapy
  - Gall stones

Common Mistakes

- “Other” category:
  - Cyclosporine toxicity
  - Chemotoxicity
  - Cholestatic jaundice
  - Hemolysis
  - Gall bladder sludge
  - Sepsis
Specify Diagnosis of Liver Toxicity

- Questions
  - Details of clinical signs and symptoms
    - Ascitis, enlarged/painful liver, weight gain
  - Details of evaluation
    - Bilirubin, liver enzymes, liver ultrasound/doppler, biopsy
  - “Other” category
    - Features that may be used diagnose liver toxicity such as CAH, Hepatitis B or C infection

Other Organ Impairment

- Questions
  - Clinically significant complications are listed
    - Yes/No variable and date of diagnosis
  - Note the following:
    - Diabetes/hyperglycemia: please do not report transient steroid-induced diabetes/hyperglycemia
    - Only hemorrhagic cystitis requiring medical intervention as noted on the Form

Complications: Other Organs

- Endocrine
  - Usually late on-set
  - Growth failure
  - Gonadal dysfunction/infertility
  - Hypothyroidism
- Renal
  - TTP, HUS, renal failure requiring dialysis
- Cardiac
  - CHF, <40% ejection fraction
Common Mistakes

- “Other” category:
  - Sepsis
  - Ascitis, electrolyte abnormalities
  - Blurred vision, conjunctivitis
  - Atrial fibrillation/flutter/STV/
    Cardiomyopathy
  - See question: CHF and EF <40%
  - Migraine
  - Mucositis

Follow-up Forms

- Day 100 (Form 130)
- 6 months- 2 years (Form 140)
- Follow-up beyond 2 years (Form 150)
  - Similar questions except the Form 150
    requests limited information on IPN, DAH,
    BO and VOD
  - Questions related to other organ
    impairment are similar across the 3
    versions