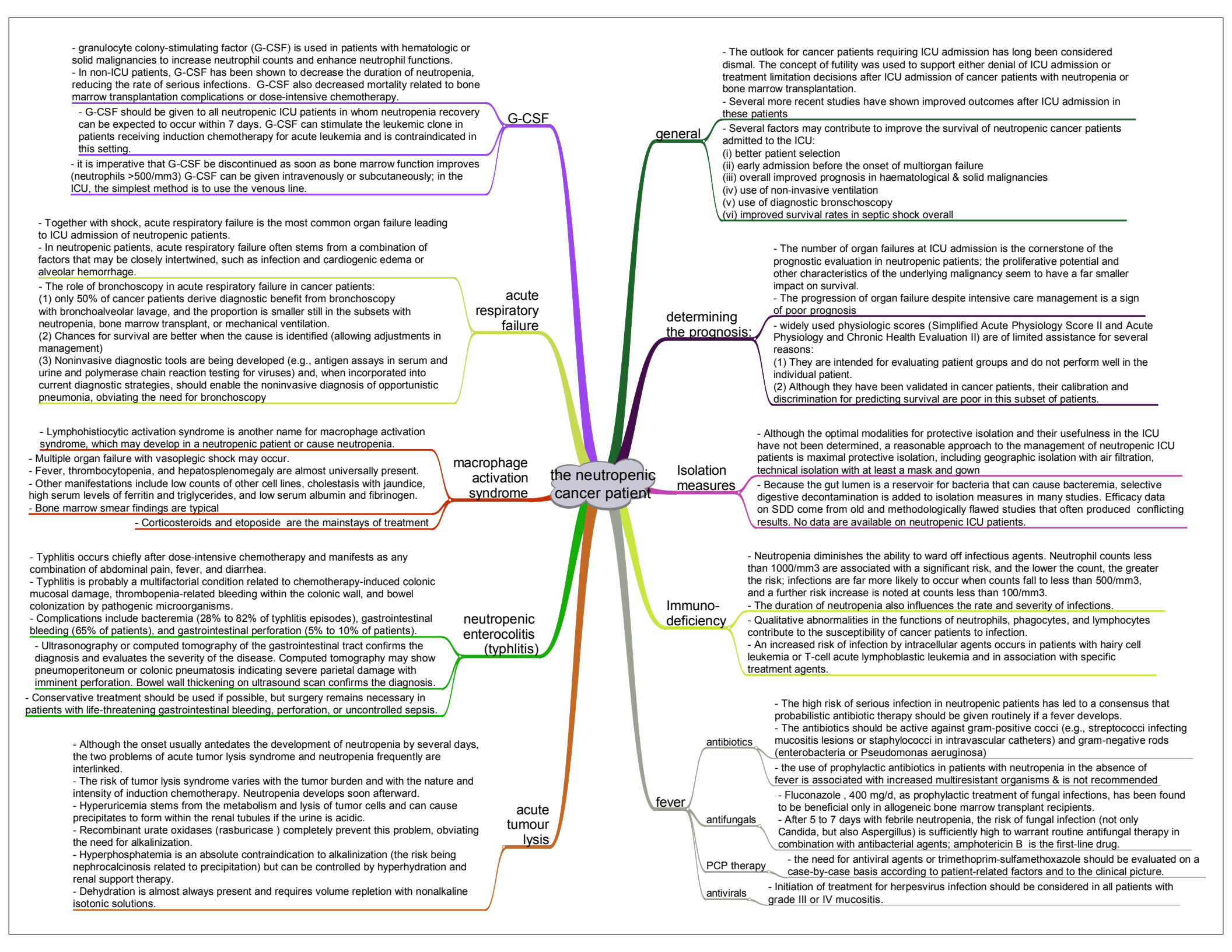
the neutropenic cancer patient
G-CSF
- granulocyte colony-stimulating factor (G-CSF) is used in patients with hematologic or solid malignancies to increase neutrophil counts and enhance neutrophil functions.
- In non-ICU patients, G-CSF has been shown to decrease the duration of neutropenia, reducing the rate of serious infections. G-CSF also decreased mortality related to bone marrow transplantation complications or dose-intensive chemotherapy.
- G-CSF should be given to all neutropenic ICU patients in whom neutropenia recovery can be expected to occur within 7 days. G-CSF can stimulate the leukemic clone in patients receiving induction chemotherapy for acute leukemia and is contraindicated in this setting.
- it is imperative that G-CSF be discontinued as soon as bone marrow function improves (neutrophils >500/mm3) G-CSF can be given intravenously or subcutaneously; in the ICU, the simplest method is to use the venous line.
acute respiratory failure
- Together with shock, acute respiratory failure is the most common organ failure leading to ICU admission of neutropenic patients.
- In neutropenic patients, acute respiratory failure often stems from a combination of factors that may be closely intertwined, such as infection and cardiogenic edema or alveolar hemorrhage.
- The role of bronchoscopy in acute respiratory failure in cancer patients:
(1) only 50% of cancer patients derive diagnostic benefit from bronchoscopy with bronchoalveolar lavage, and the proportion is smaller still in the subsets with neutropenia, bone marrow transplant, or mechanical ventilation.
(2) Chances for survival are better when the cause is identified (allowing adjustments in management)
(3) Noninvasive diagnostic tools are being developed (e.g., antigen assays in serum and urine and polymerase chain reaction testing for viruses) and, when incorporated into current diagnostic strategies, should enable the noninvasive diagnosis of opportunistic pneumonia, obviating the need for bronchoscopy
macrophage activation syndrome
- Lymphohistiocytic activation syndrome is another name for macrophage activation syndrome, which may develop in a neutropenic patient or cause neutropenia.
- Multiple organ failure with vasoplegic shock may occur.
- Fever, thrombocytopenia, and hepatosplenomegaly are almost universally present.
- Other manifestations include low counts of other cell lines, cholestasis with jaundice, high serum levels of ferritin and triglycerides, and low serum albumin and fibrinogen.
- Bone marrow smear findings are typical
- Corticosteroids and etoposide are the mainstays of treatment
neutropenic enterocolitis (typhlitis)
- Typhlitis occurs chiefly after dose-intensive chemotherapy and manifests as any combination of abdominal pain, fever, and diarrhea.
- Typhlitis is probably a multifactorial condition related to chemotherapy-induced colonic mucosal damage, thrombopenia-related bleeding within the colonic wall, and bowel colonization by pathogenic microorganisms.
- Complications include bacteremia (28% to 82% of typhlitis episodes), gastrointestinal bleeding (65% of patients), and gastrointestinal perforation (5% to 10% of patients).
- Ultrasonography or computed tomography of the gastrointestinal tract confirms the diagnosis and evaluates the severity of the disease. Computed tomography may show pneumoperitoneum or colonic pneumatosis indicating severe parietal damage with imminent perforation. Bowel wall thickening on ultrasound scan confirms the diagnosis.
- Conservative treatment should be used if possible, but surgery remains necessary in patients with life-threatening gastrointestinal bleeding, perforation, or uncontrolled sepsis.
acute tumour lysis
- Although the onset usually antedates the development of neutropenia by several days, the two problems of acute tumor lysis syndrome and neutropenia frequently are interlinked.
- The risk of tumor lysis syndrome varies with the tumor burden and with the nature and intensity of induction chemotherapy. Neutropenia develops soon afterward.
- Hyperuricemia stems from the metabolism and lysis of tumor cells and can cause precipitates to form within the renal tubules if the urine is acidic.
- Recombinant urate oxidases (rasburicase ) completely prevent this problem, obviating the need for alkalinization.
- Hyperphosphatemia is an absolute contraindication to alkalinization (the risk being nephrocalcinosis related to precipitation) but can be controlled by hyperhydration and renal support therapy.
- Dehydration is almost always present and requires volume repletion with nonalkaline isotonic solutions.
general
- The outlook for cancer patients requiring ICU admission has long been considered dismal. The concept of futility was used to support either denial of ICU admission or treatment limitation decisions after ICU admission of cancer patients with neutropenia or bone marrow transplantation.
- Several more recent studies have shown improved outcomes after ICU admission in these patients
- Several factors may contribute to improve the survival of neutropenic cancer patients admitted to the ICU:
(i) better patient selection
(ii) early admission before the onset of multiorgan failure
(iii) overall improved prognosis in haematological & solid malignancies
(iv) use of non-invasive ventilation
(v) use of diagnostic bronschoscopy
(vi) improved survival rates in septic shock overall
determining the prognosis:
- The number of organ failures at ICU admission is the cornerstone of the prognostic evaluation in neutropenic patients; the proliferative potential and other characteristics of the underlying malignancy seem to have a far smaller impact on survival.
- The progression of organ failure despite intensive care management is a sign of poor prognosis
- widely used physiologic scores (Simplified Acute Physiology Score II and Acute Physiology and Chronic Health Evaluation II) are of limited assistance for several reasons:
(1) They are intended for evaluating patient groups and do not perform well in the individual patient.
(2) Although they have been validated in cancer patients, their calibration and discrimination for predicting survival are poor in this subset of patients.
Isolation measures
- Although the optimal modalities for protective isolation and their usefulness in the ICU have not been determined, a reasonable approach to the management of neutropenic ICU patients is maximal protective isolation, including geographic isolation with air filtration, technical isolation with at least a mask and gown
- Because the gut lumen is a reservoir for bacteria that can cause bacteremia, selective digestive decontamination is added to isolation measures in many studies. Efficacy data on SDD come from old and methodologically flawed studies that often produced conflicting results. No data are available on neutropenic ICU patients.
Immuno-deficiency
- Neutropenia diminishes the ability to ward off infectious agents. Neutrophil counts less than 1000/mm3 are associated with a significant risk, and the lower the count, the greater the risk; infections are far more likely to occur when counts fall to less than 500/mm3, and a further risk increase is noted at counts less than 100/mm3.
- The duration of neutropenia also influences the rate and severity of infections.
- Qualitative abnormalities in the functions of neutrophils, phagocytes, and lymphocytes contribute to the susceptibility of cancer patients to infection.
- An increased risk of infection by intracellular agents occurs in patients with hairy cell leukemia or T-cell acute lymphoblastic leukemia and in association with specific treatment agents.
fever
antibiotics
- The high risk of serious infection in neutropenic patients has led to a consensus that probabilistic antibiotic therapy should be given routinely if a fever develops.
- The antibiotics should be active against gram-positive cocci (e.g., streptococci infecting mucositis lesions or staphylococci in intravascular catheters) and gram-negative rods (enterobacteria or Pseudomonas aeruginosa)
- the use of prophylactic antibiotics in patients with neutropenia in the absence of fever is associated with increased multiresistant organisms & is not recommended
antifungals
- Fluconazole , 400 mg/d, as prophylactic treatment of fungal infections, has been found to be beneficial only in allogeneic bone marrow transplant recipients.
- After 5 to 7 days with febrile neutropenia, the risk of fungal infection (not only Candida, but also Aspergillus) is sufficiently high to warrant routine antifungal therapy in combination with antibacterial agents; amphotericin B is the first-line drug.
PCP therapy
- the need for antiviral agents or trimethoprim-sulfamethoxazole should be evaluated on a case-by-case basis according to patient-related factors and to the clinical picture.
antivirals
- Initiation of treatment for herpesvirus infection should be considered in all patients with grade III or IV mucositis.