Infection is the most common complication associated with febrile neutropenia and accounts for substantial morbidity and mortality. The principles that guide the management of patients with febrile neutropenia are different from those for immunocompetent patients. A consensus conference for establishing guidelines for management of febrile neutropenia in Taiwan was held on March 12, 2005, following a symposium on febrile neutropenia held in conjunction by the Infectious Diseases Society of Taiwan, the Hematology Society of Taiwan, the Medical Foundation in Memory of Dr. Deh-Lin Cheng, Foundation of Professor Wei-Chuan Hsieh for Infectious Diseases Research and Education, and CY Lee’s Research Foundation for Pediatric Infectious Diseases and Vaccine. Participants of the consensus meeting included board members of the Society, and experts in infectious diseases, hematologists, oncologists and microbiologists.* Three principles are maintained in establishing these guidelines:

1. Guidelines follow the main structure of the Infectious Diseases Society of America’s guidelines.

2. Guidelines are based on local epidemiology and susceptibility patterns of pathogens.

3. Antimicrobial agents recommended in the guidelines are agents already marketed in Taiwan.

Special considerations are given to include tuberculosis due to its high prevalence in Taiwan, although admittedly it is a relatively uncommon pathogen of febrile neutropenia. Recommendations on tuberculosis are based solely on expert opinion, and may be subject to change in the future with the availability of local epidemiologic data or studies. Many recommendations are still based on expert opinion and unpublished data, due to lack of well-designed, randomized, controlled, clinical trials in this region.

These guidelines are approved by the board of Infectious Diseases Society of Taiwan, and a copy will be sent to primary care physicians in hospitals. The guidelines are published in the Journal of Immunology, Microbiology and Infection, to serve as an easily accessible reference to all practicing physicians in Taiwan.

Algorithm for initial management of patients with febrile neutropenia
Febrile neutropenia guidelines

Afebrile within first 3-5 days of treatment

No etiology identified

Low risk

Change to:
- a newer fluoroquinolone
- amoxicillin-clavulanate or amoxicillin-sulbactam (adults)
- cefixime (children)

High risk

Continue same antibiotics

Etiology identified

Adjust to most appropriate treatment based on susceptibility data

Persistent fever during first 3-5 days of treatment: no etiology

Reassess patient on days 3-5

- If no change in patient’s condition (consider stopping glycopeptide)
  
  Continue initial antibiotics

- If progressive disease
  
  Change antibiotics

- If febrile through days 5-7 and resolution of neutropenia is not imminent
  
  Antifungal drug, with or without antibiotic change

Duration of antibiotic therapy

Afebrile by day 3-5

- ANC ≥500/mm³ for 2 consecutive days
  
  Stop antibiotics 48 h after afebrile
  
  ANC ≥500 cells/mm³

- ANC <500/mm³ by day 7
  
  Initial low risk, clinically well
  
  Stop when afebrile for 5-7 days

- Initial high risk
  
  Stop when afebrile for 5-7 days

Persistent fever

- ANC ≥500 cells/mm³
  
  Stop 4-5 days

- ANC <500 cells/mm³
  
  Reassess

- ANC <500/mm³
  
  Continue for 2 weeks

- ANC <500 cells/mm³
  
  Stop if no disease and condition stable
Evaluation of tuberculosis (TB) in patients with febrile neutropenia (FN)

Febrile neutropenic patients

CXR

Abnormal

Active TB

Old TB or nonspecific changes

Evaluate for active TB:
Sputum acid-fast stain and culture, PCR...

FUO

Normal

Anti-TB therapy

Persistent fever >2 weeks

Abbreviations: ANC = absolute neutrophil count; CXR = chest radiography; PCR = polymerase chain reaction; FUO = fever of unknown origin

a Indicates a single oral temperature of ≥38.3°C or an oral temperature of ≥38.0°C for ≥1 h or a single ear probe temperature of ≥38.3°C.

b Indicates a neutrophil count of <500 cells/mm³ or a count of <1000 cells/mm³ with a predicted decrease to <500 cells/mm³.

c Factors that favor a low risk for severe infection among patients with neutropenia are: absolute neutrophil count of ≥100 cells/mm³; absolute monocyte count of ≥100 cells/mm³; normal findings on a chest radiograph; nearly normal results of hepatic and renal function tests; duration of neutropenia of <7 days; resolution of neutropenia expected in <10 days; no intravenous catheter-site infection; early evidence of bone marrow recovery; malignancy in remission; peak temperature of <39°C; no neurologic or mental changes; no appearance of illness; no abdominal pain; no ecthyma gangrenosum; and no comorbidity complications (vomiting, diarrhea, shock, hypoxia, pneumonia, other deep organ infection).

d Ciprofloxacin, levofloxacin, moxifloxacin.

e First-, second-, third-generation cephalosporins.

f Vancomycin, teicoplanin.

g Imipenem, meropenem.

h Amikacin, isepamicin.

*Consensus conference participants (in alphabetical order):