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 Many recommendations are still based on expert opinion and unpublished data, due to lack of well-designed, randomized, controlled, clinical trials in this region.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

1. **Fever** (temperature 38.3°C) + **Neutropenia** (<500 neutrophils/mm³)

   - **Low risk**
     - Oral
       - A newer fluoroquinolone⁷ + amoxicillin-clavulanate or ampicillin-sulbactam (adults)
       - Cefixime (children)

   - **High risk**
     - Intravenous
       - A cephalosporin⁸ + an aminoglycoside
       - Monotherapy (A)
         - Cefepime, cefpirome, piperacillin-tazobactam or a carbapenem?
       - Two drug (B)
         - An aminoglycoside⁹ + ceftazidime, piperacillin-tazobactam, cefepime, cefpirome or a carbapenem?

   - Glycopeptide¹ need not be needed
   - Glycopeptide¹ needed

   - Reassess after 3-5 days
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

Discharge

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)
- If progressive disease
- If criteria for glycopeptide are met

Continue initial antibiotics

Change antibiotics

Antifungal drug, with or without antibiotic change

Duration of antibiotic therapy

Afebrile by day 3-5

ANC $\geq 500$ cells/mm$^3$ by day 7

Initial low risk

- Initial high risk

ANC $<100$ cell/mm$^3$, mucositis, unstable signs

Stop antibiotics 48 h after afebrile

ANC $\geq 500$ cells/mm$^3$

Stop when afebrile for 5-7 days

Continue antibiotics

Stop if no disease and condition stable

Persistent fever

ANC $<500$ cells/mm$^3$

Stop 4-5 days

Reassess

Reassess

ANC $\geq 500$ cells/mm$^3$

Continue for 2 weeks

Stop antibiotics

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Evaluation of tuberculosis (TB) in patients with febrile neutropenia (FN)

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

\( ^a \) Indicates a single oral temperature of \( \geq 38.3 \)°C or an oral temperature of \( \geq 38.0 \)°C for \( \geq 1 \) h or a single ear probe temperature of \( \geq 38.3 \)°C.

\( ^b \) Indicates a neutrophil count of <500 cells/mm\(^3\) or a count of <1000 cells/mm\(^3\) with a predicted decrease to <500 cells/mm\(^3\).

\( ^c \) Factors that favor a low risk for severe infection among patients with neutropenia are: absolute neutrophil count of \( \geq 100 \) cells/mm\(^3\); absolute monocyte count of \( \geq 100 \) cells/mm\(^3\); 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):