

# Antibiotics usage and prophylaxis for children

## Antibiotics usage and prophylaxis for children

**Introduction:** At least 85% of pathogens associated with fever and neutropenia are bacteria, the most common being *Pseudomonas aeruginosa*, *Escherichia coli*, *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Streptococcus* species. *Serratia* species and *Enterobacter* species are now also being seen. Consider coagulase-negative staphylococci, *Bacillus* species and fungi in patients with central venous catheters.

**Prevention of infection** Neutropenia alone is not a sufficient indication for hospitalisation.

When hospitalisation is necessary, patients should be reverse barrier-nursed if possible.

Patients can attend school when the absolute neutrophil count (ANC) is  $\geq 2 \times 10^9/L$ .

For protection of the anal rectal mucosa:

prevent constipation,

avoid rectal suppositories.

Prophylaxis against bacteria: **Splenectomized children:** Phenoxymethylpenicillin or erythromycin is given indefinitely.

Dosage: oral,  $\leq 3$  years, 125 mg twice daily,

$\geq 3$  years, 250 mg twice daily. **Vaccination before splenectomy:**

Polyvalent pneumococcal vaccine, 0.5 mL IM for children  $\geq 2$  years.

*Haemophilus b* conjugated vaccine, 0.5 mL IM for infants  $\geq 2$  months; children under 12 months; 15 months require a course of 3 injections, and the manufacturer's instructions should be followed.

Prophylaxis against viruses: Decrease exposure; do not administer live attenuated oral polio vaccine to the siblings of patients receiving chemotherapy. Killed polio vaccine may be given.

Notify appropriate teachers, caregivers and friends of the risk of infection with the varicella-zoster virus.

Prophylaxis against varicella-zoster virus with varicella-zoster immunoglobulin (ZIG): Indications: Patients on chemotherapy or off therapy for  $\geq 12$  months, exposed to an individual with varicella/zoster infection within the household or any indoor contact of one hour or longer. ZIG may be administered up to 96 hours after exposure (preferably within 72 hours). If varicella develops, all chemotherapy should be stopped. Administer: Aciclovir, IV, 1 500 mg/m<sup>2</sup>/day in 3 divided doses for 10 days. **Prophylaxis against *Pneumocystis carinii*:** Patients on aggressive chemotherapy regimens in whom the absolute neutrophil count (ANC) can be expected to be less than  $0.5 \times 10^9/L$  for more than 14 days should take: Trimethoprim/sulfamethoxazole, oral, 5 mg trimethoprim + 25 mg

sulfamethoxazole/kg/24 hours in 2 divided doses for 3 days per week. **Prophylaxis against fungi:** In patients with leukaemia and lymphomas, prophylactic nystatin suspension, oral, 100 000 units 6 hourly is used for the duration of the induction phase. **Prophylaxis in patients with central catheters:** All patients with in-dwelling central catheters (either the external catheter type or the subcutaneous reservoir type) should receive prophylaxis against bacterial endocarditis during invasive procedures, including operations on the gastrointestinal or genito-urinary tract, endotracheal intubation and dental manipulation. See prophylaxis against bacterial endocarditis, page 70. Initial empiric management of the child with febrile neutropenia **Definitions:** Neutropenia is defined as an absolute neutrophil count (ANC) less than  $0.5 \times 10^9/L$ , or less than  $1 \times 10^9/L$  and falling.

Fever is defined as a temperature of  $38.0^\circ C$  occurring 3 times in 24 hours or a single oral temperature  $\geq 38.5^\circ C$ . (Rectal temperatures are contraindicated in the setting of neutropenia).

Antibiotics: The specific antibiotic regimen for an individual patient will depend on:

whether or not the patient has a central venous access device, antibiotic sensitivity of bacterial isolates from patients in the unit, drug allergy, renal and hepatic dysfunction, other concomitant nephrotoxic, hepatotoxic or ototoxic drugs.

**Empiric therapy:** After appropriate investigations, commence therapy with combination of an aminoglycoside (amikacin or gentamicin) plus an antipseudomonal beta-lactam antibiotic (ceftazidime) for 10-14 days. Dosages; see table opposite.

**Anaerobic therapy:** If the patient already has severe mucositis or gingivitis, peri-anal discomfort, diarrhoea or abdominal pain at the onset of first fever, an anaerobic infection may be present. Add clindamycin or metronidazole to the empiric regimen, for 10-14 days. Dosages; see table opposite.

**Vancomycin:** If a central venous catheter is in position or if methicillin-resistant *Staphylococcus aureus*, beta-lactam resistant *Staphylococcus epidermidis* or *viridans* streptococci are suspected, add vancomycin for 10-14 days. Dosage; see table opposite.

**Oesophagitis:** Add antifungal therapy (amphotericin B or fluconazole) and/or aciclovir for 10-14 days for possible herpes virus infection. Dosages see table opposite.

**Diffuse pulmonary infiltrate:** Treat with trimethoprim/sulfamethoxazole combination and erythromycin for 10-14 days. Dosages; see table opposite. (Trimethoprim/sulfamethoxazole can be given orally when the patient is stable.)

Dosages of antibiotics used in management of febrile neutropenia (all doses are given for the IV route) **Drug**

Total daily dose

Dosage interval Amikacin

15 mg/kg/24 hours

once daily or divided 12 hourly Gentamicin

4 mg/kg/24 hours

divided 12 hourly Ceftazidime

100-150 mg/kg/24 hours (max. 6 g/24 hours)

divided 8 hourly Metronidazole

30 mg/kg/24 hours

divided 6 hourly Clindamycin

30 mg/kg/24 hours

divided 6 hourly Vancomycin

40 mg/kg/24 hours (max. 2 g/24 hours)

divided 6 hourly Amphotericin B

0.6 mg/kg/24 hours

4-hour infusion Fluconazole

3-12 mg/kg/24 hours

single daily dose Aciclovir

30 mg/kg/24 hours

divided 8 hourly Trimethoprim / sulfamethoxazole

20 / 100 mg/kg/24 hours

divided 6- 8 hourly Erythromycin

50 mg/kg/24 hours

divided 6 hourly **If no specific pathogen is identified on culture:** Continue empiric broad-spectrum antibiotic coverage until the fever has settled and the granulocyte count is greater than  $1.5 \times 10^9/L$  on 2 consecutive days.

If the fever settles on antibiotics but granulocytopenia persists, stop antibiotics after 10-14 days.

If granulocytopenia persists, and an afebrile patient again becomes febrile, consider changing empiric broad-spectrum antibiotic coverage and adding antifungal therapy.

If fever and granulocytopenia persist on empiric broad-spectrum antibiotic therapy for 3-7 days, antibiotic coverage may need to be broadened to include vancomycin or better anaerobic coverage (clindamycin or metronidazole). Aciclovir should be considered in the patient with mucositis, painful gingivitis or symptoms of oesophagitis. If the patient continues to be febrile, amphotericin B should be initiated probably no later than day 7.

If a specific pathogen is identified on culture: Tailor antibiotic therapy to the specific pathogen and sensitivity for 10-14 days or until the ANC is greater than  $1.5 \times 10^9/L$ .

Continue antibiotic therapy for a minimum of 10 days (14 days if an indwelling venous catheter is present) for an uncomplicated infection, and for as long as 6 weeks for fungal infections, osteomyelitis or peri-anal cellulitis.

The management of fever without neutropenia **When a central venous catheter is not present:** If a specific infection is not documented, continue to monitor clinically and with daily blood cultures and other relevant laboratory studies, but do not start antibiotics.

When a specific pathogen is isolated treat with specific antibiotics.

When a central venous catheter is present: If only an exit-site infection is suspected, obtain blood cultures from all catheter ports, one venepuncture site (if practical), and the exit site.

Begin antibiotic therapy with: Flucloxacillin, oral, 50 mg/kg/24 hours in 4 divided doses (6 hourly).

Reassess at 24-48 hours.

If improved, finish 10-day course of antibiotic therapy.

If not improved after 48 hours of flucloxacillin, begin therapy with: Vancomycin, IV, 40 mg/kg/24 hours in 3 divided doses (8 hourly).

If not improved after 72 hours of parenteral therapy, change antibiotics or consider removing the catheter.

If there is no evidence of local infection, obtain blood cultures from all catheter ports and one venepuncture site.

Consider commencement of parenteral therapy with: Vancomycin, IV, 40 mg/kg/24 hours in 3 divided doses (8 hourly) (maximum 2 g/24 hours) AND

Gentamicin, IV, 6 mg/kg/24 hours in 3 divided doses (8 hourly).

Reassess at 24-hour intervals.

If the cultures are negative, stop antibiotic therapy after 72 hours.

If the cultures are positive and remain positive after 72 hours, change antibiotics or consider removing the catheter.

If the cultures become negative, complete a 10-14 day course of antibiotics and do not remove the catheter.