Chloramphenicol

- Broad spectrum
- Very widely distributed.
- Very effective, no resistance.
- Very toxic. (the gray-baby syndrome)
- Disrupt function of 50S ribosomal subunits to reversibly inhibit protein synthesis.

Gray baby syndrome is a rare but serious side effect that occurs in newborn infants (especially premature babies) following the accumulation of antibiotic chloramphenicol.

Chloramphenicol

- Was the drug of choice for Salmonella(Typhoid Fever), but replaced by safer drugs.
- Still used for meningitis caused by *H. influenzea.*
- Aplastic anemia:
  - Incidence is common 1/40,000.
  - Delayed for a few months after intake.
  - Fatal.

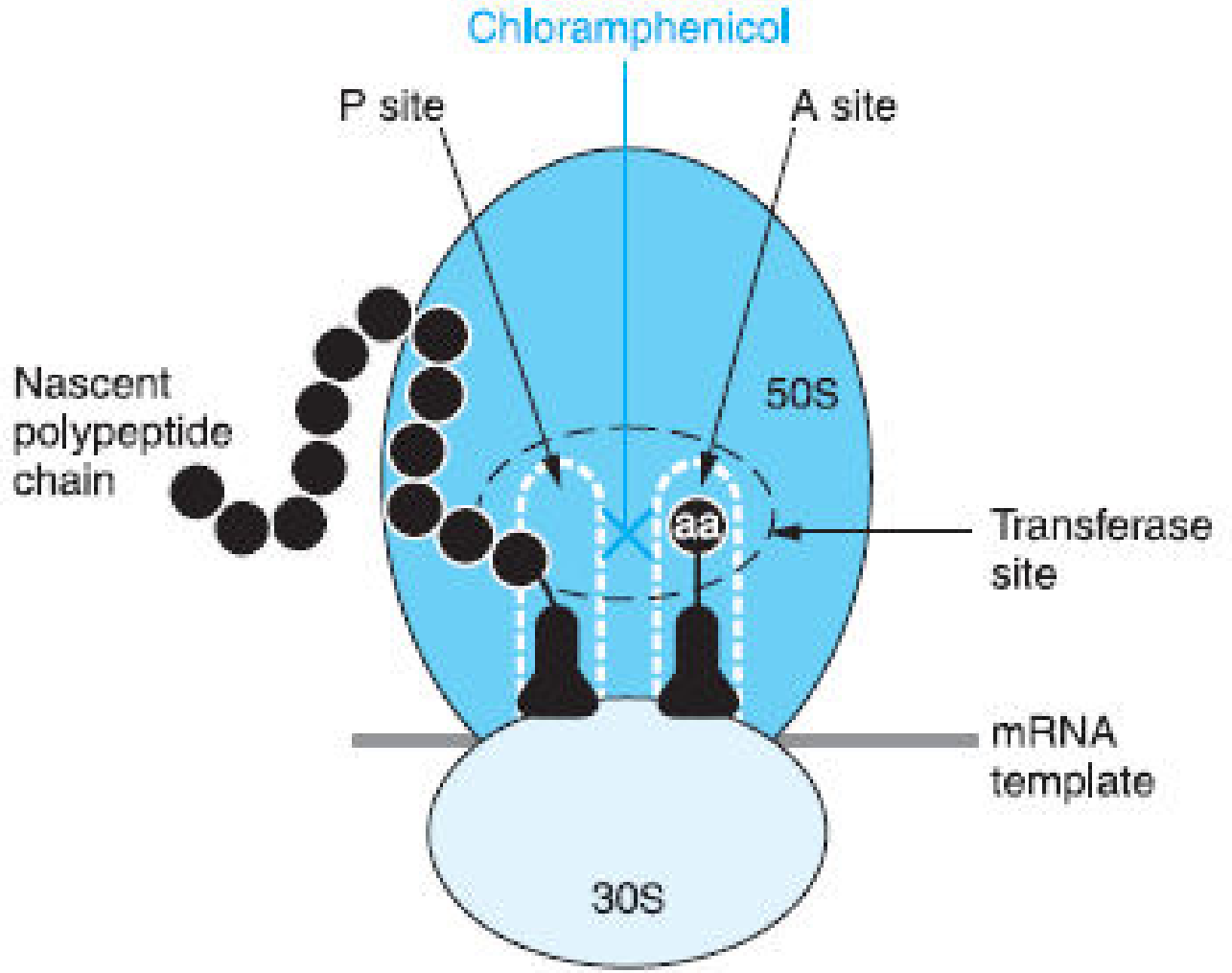

Figure 46–2. Inhibition of bacterial protein synthesis by chloramphenicol. Chloramphenicol binds to the 50S ribosomal subunit at the peptidyltransferase site and inhibits the transpeptidation reaction.

transpeptidation reaction
A reaction involving the transfer of one or more amino acids from one peptide chain to another,

Mechanism of Action

- Chloramphenicol (Chloromycetin) is a nitrobenzene derivative that affects protein synthesis by binding to the 50S ribosomal subunit preventing peptide bond formation.

- It prevents the attachment of the amino acid end of aminoacyl-tRNA to the A site, hence the association of peptidyltransferase with the amino acid substrate.

Mechanism of Action

- Resistance due to changes in the ribosome binding site results in
  - ❖ a decreased affinity for the drug,
  - ❖ decreased permeability,
  - ❖ and plasmids that code for enzymes
- that degrade the antibiotic.
- The drug-induced inhibition of mitochondrial protein synthesis is probably responsible for the associated toxicity.

Antibacterial Spectrum

- Chloramphenicol is a broad-spectrum antibiotic that is effective against gram-positive and gram-negative bacteria, including Rickettsia, Mycoplasma, and Chlamydia spp.

- Chloramphenicol is also effective against most anaerobic bacteria, including Bacteroides fragilis.

Absorption, Distribution, Metabolism, and Excretion

- Chloramphenicol is rapidly and completely absorbed from the gastrointestinal tract and is not affected by food ingestion or metal ions.
- Parenteral administration

is generally reserved for situations in which oral therapy is contraindicated, as in the treatment of meningitis and septicemia or when vomiting prohibits oral administration

Absorption, Distribution, Metabolism, and Excretion

- The biological half-life of chloramphenicol is 1.5 to 3.5 hours. Although up to 60% of the drug is bound to serum albumin, it penetrates the brain and CSF and crosses the placental barrier.
- Chloramphenicol is inactivated in the liver by glucuronosyltransferase and is rapidly excreted (80–90% of dose) in the urine.

Clinical Uses

The potentially fatal nature of chloramphenicolinduced bone marrow suppression restricts its use to a few life-threatening infections in which the benefits outweigh the risks. There is no justification for its use in treating minor infections.

Chloramphenicol is no longer recognized as the treatment of choice for any bacterial infection. In almost all instances, other effective antimicrobial agents are available.

Since effective CSF levels are obtained, it used to be a choice for treatment of specific bacterial causes of meningitis:

- Haemophilus influenzae,
- Neisseria meningitidis,
- and S. pneumoniae

Additionally, it was effective against H. influenzae–related arthritis, osteomyelitis, and epiglottitis.

- The development of B-lactamase-producing strains of H. influenzae increased the use of chloramphenicol.

- However, with the advent of third-generation cephalosporins such as ceftriaxone and cefotaxime, chloramphenicol use has significantly decreased.
- If the patient is hypersensitive to B-lactams, chloramphenicol administration is appropriate therapy for meningitis caused by N. meningitidis and S. pneumoniae.

- Chloramphenicol remains a major treatment of typhoid and paratyphoid fever in developing countries.

- However, with increasing resistance to ampicillin, trimethoprim-sulfamethoxazole and, to some extent, chloramphenicol, fluoroquinolones and some third-generation cephalosporins (e.g., ceftriaxone) have become the drugs of choice

- Chloramphenicol also is widely used for the topical treatment of eye infections.
- It is a very effective agent

because of its extremely broad spectrum of activity and its ability to penetrate ocular tissue.

- The availability of

safer, less irritating instilled ophthalmic antibiotics and the increase in fatal aplastic anemia associated with the use of this dosage form suggest that this agent might best be withdrawn.

- Chloramphenicol is an alternative to tetracycline for rickettsial diseases, especially in children younger than 8 years,
- alone or in combination with other antibiotics,

it has been used to treat vancomycin-resistant enterococci.

- Another indication for chloramphenicol is in

the treatment of serious anaerobic infections caused by penicillin-resistant bacteria, such as B. fragilis