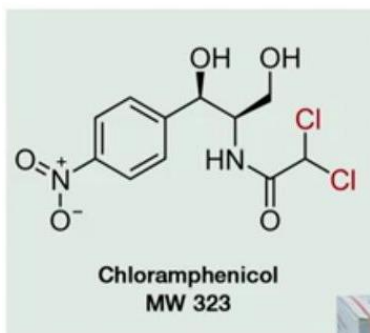


Dr. AM Fouad MB, PhD



## Chloramphenicol:

- Because of its toxicity, its use is restricted to life-threatening infections for which no alternatives exist. Can be given orally or I.V. now used topically.
- Eliminated by liver metabolism .
- Is very effective in typhoid fevers.



Dr. AM Fouda MD, PhD



## Mechanism of action

- Passively enter & bind reversibly to the bacterial 50s ribosome subunit.
- Inhibits peptidyl transferase reaction → prevents formation of peptide bonds- (Transpeptidation)
- At high doses, it inhibits protein synthesis in host cell mitochondria via a similar mechanism, because of similarity to bacterial ribosomes; erythropoietic cells are particularly sensitive.

## Pharmacokinetics

Chloramphenicol is a lipophilic drug , orally absorbed and can be given by parenteral routes . It is widely distributed throughout the body and penetrate to CSF. It is conjugated in liver to inactive glucuronide, about 10% of the total dose administered, and its inactive products are eliminated in the urine. Dose reductions are necessary in patients with liver

dysfunction or cirrhosis. It is also **secreted into breast milk** and should be avoided in breast feeding mothers.

### **Clinical uses:**

Because of its toxicity, it only may be considered for treatment of serious rickettsial infections such as **typhus and Rocky Mountain spotted fever**. It is an alternative to a  $\beta$ -lactam antibiotic for treatment of bacterial meningitis occurring in patients who have major hypersensitivity reactions to penicillin.

### ***Adverse effects:***

1- **Anemias**: Patients may experience dose-related anemia, hemolytic anemia e.g; in patients with G-6- PD deficiency, and aplastic anemia.

2- **Gray baby syndrome**: Neonates have a low capacity to glucuronidate the antibiotic, and they have underdeveloped renal function. Therefore, neonates have a decreased ability to excrete the drug, which accumulates to levels that interfere with the function of mitochondrial ribosomes. This leads to poor feeding, depressed breathing, cardiovascular collapse, cyanosis (hence the term “gray baby”), and death. Adults who have received very high doses of the drug can also exhibit this toxicity.

3- **Superinfection, GIT disturbance and hypersensitivity**.

### **Drug interactions:**

Chloramphenicol inhibits some of the hepatic mixed-function oxidases and, thus, **blocks the metabolism** of drugs such as **warfarin and phenytoin**, thereby elevating their concentrations and potentiating their effects.

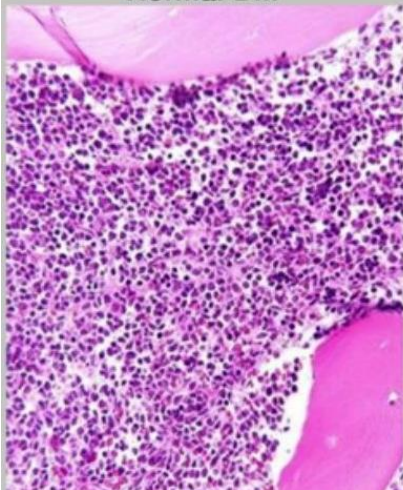
# Gray baby syndrome

Gray-bluish skin  
Cyanosis  
CVS collapse  
Abdominal distension  
Irregular respiration

Dr. AM Fouda MD, PhD  
Antimicrobial Chemotherapy - Lecture 09: Chloramphenicol



Normal BM



BM suppression

