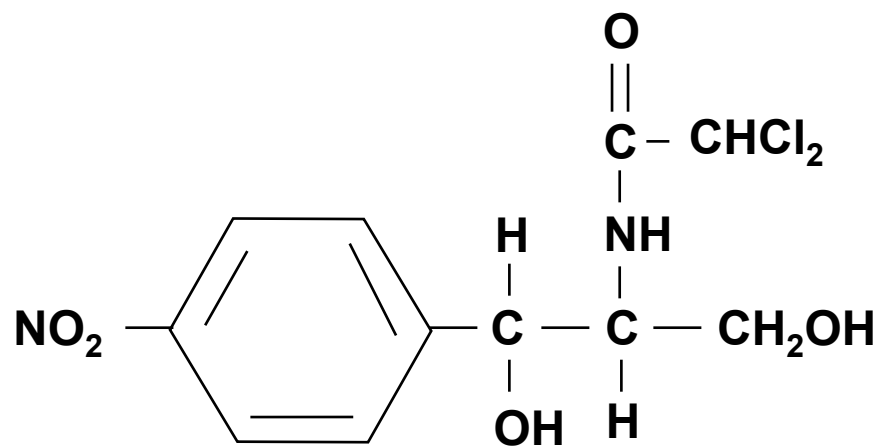


Chloramphenicol





Mechanism of Action

- ❑ actively transported into cell
- ❑ binds to 50S subunit of 70S ribosome & prevents binding of tRNA
- ❑ inhibits protein synthesis (bacteriostatic against many organisms (in vitro bactericidal against *H. influenzae*, most *S. pneumoniae*, *N. meningitidis* but not Grp B Strep or enteric organisms))

Resistance

- ❑ Cell impermeability to chloramphenicol
- ❑ Enzyme production → chloramphenicol acetylation (inactivation)



Chloramphenicol

Gram Positive

- ❑ *S. aureus*, *S. epidermidis*
(β -lactamase producing, not (MRSA))
- ❑ *S. pyogenes*, ***S. pneumoniae***, *S. viridans*
Grp B Strep (1-2% resistant)
- ❑ *L. monocytogenes*, *C. diphtheria*



...Spectrum

Gram Negative

- ❑ *H. influenzae*, *E. coli*, Enterobacter, Klebsiella, Proteus, Serratia, Citrobacter, Providencia,
- ❑ *N. meningitidis*, *N. gonorrhoeae*
- ❑ **Salmonella**, **Shigella**, *Y. enterocolitica*, *Y. pestis*

Anaerobes

- ❑ most sensitive (gram **+** and gram **-**)
- ❑ Particularly ***B. fragilis***
- ❑ **Others-** Mycoplasma, Chlamydia, *T. pallidum*, **Rickettsia**, Leptospira



Forms of Administration

Oral

- ❑ absorbed well orally in adults, unpredictable in pediatrics
- ❑ palmitate suspension hydrolyzed in intestine to active drug

Intravenous / Intramuscular

- ❑ inactive succinate ester -hydrolyzed in body (incomplete hydrolysis - levels only 70% of those after oral administration)
- ❑ Intramuscular well tolerated
- ❑ I.M. peak similar to I.V. (one study only 1/2-1/3 with some clinical failures - not recommended)

Eye Drop



Distribution, Metabolism, Excretion

- ❑ diffuses well into many tissues and fluids
- ❑ **CSF** 30-50% of serum levels even without inflammation

Metabolized ***primarily by liver → inactive glucuronide
(excreted in kidney)

- ❑ Infants and children have reduced capacity for glucuronidation (must ↓ dose)***
- ❑ may be 3 fold variation in same age group
- ❑ only 5-10% unchanged in urine
- ❑ t_{1/2} in adults 4.1 hr (unchanged in renal failure)
- ❑

Dosing

Neonates < 1 week	25 mg/kg/once daily
Neonates 1-4 weeks	25 mg/kg/q12h
Older children & adults	50 mg/kg/day (q6h)
with meningitis	100 mg/kg/day (q6h)

Hepatic Failure

1 g load then 500 mg q6h (Limit to 10-14 days)

Monitoring

- particularly in neonates and patients with hepatic failure
- Peaks < 25 mcg/mL (0.5 - 1.5h post dose)
(> 25 mcg/mL - bone marrow depression
50 -100mcg/mL - gray syndrome)



Adverse Effects

Bone Marrow

1) **Reversible, Dose related**

- reticulocytopenia, anemia, leukopenia, thrombocytopenia

Risk

- Adults with > 4 g/day
- serum levels > 25 mcg/mL
(severe liver disease)

- reversible when discontinue drug



Adverse Effects

2) **Idiosyncratic Aplastic Anemia (Rare)**

- 1/24,500 - 40,800 (13 X normal risk)
- may occur weeks to months after therapy (22% concurrent)
- toxic effect mechanism unknown
- more often with oral ?
- genetic predisposition ?



Adverse Effects

Gray Syndrome

- neonates- abdominal distention, vomiting, flaccidity, cyanosis, circulatory collapse, death
- may present with unexplained metabolic acidosis
- associated with levels > 50 mcg/mL
- limit dose in neonates to 25 mg/kg/day
- exchange transfusion or charcoal hemodialysis



Adverse Effects

Optic Neuritis

- ❑ with prolonged therapy
- ❑ other neurological effects described

Other

- ❑ rashes, drug fever, anaphylaxis (rare)
- ❑ Herxheimer reaction (syphilis, brucella, typhoid)
- ❑ interference with Vitamin K synthesis

Thiamphenicol

- ❑ analog of chloramphenicol
- ❑ *p*- nitro group on benzene ring replaced with methylsulfonyl group
- ❑ spectrum of activity similar to chloramphenicol
- ❑ aplastic anemia not reported
- ❑ not available in Canada or U.S.

