

Seventy to ninety per cent of an administered dose is recovered in the urine within 24 hours. The rate of excretion is proportional to the blood level.<sup>30,32,35</sup> Five to ten per cent of the total urinary excretion is active chloramphenicol. The remainder consists of inactive aromatic nitro compounds, the glucuronide comprising the major portion. The active chloramphenicol is excreted by glomerular filtration. The filtration rates are low, indicating that the protein-bound portion does not pass the glomerular membrane. The glucuronide is excreted by the renal tubules. The clearance rate of the inactive fraction is 3 to 5 times that of creatinine. Less than 3% of the total dose is excreted in the bile, primarily as the monoglucuronide, and less than 1% of the total dose appears in the stool.

Kunin, Glazko, and Finland<sup>36</sup> studied serum levels in anuric patients. They reported that the serum half-life of active chloramphenicol was not significantly prolonged in anuric patients; however, the half-life of the metabolic products of chloramphenicol was markedly extended in patients with severe renal disease but no toxic effects were observed. The same investigators found that the serum half-life of active chloramphenicol was prolonged in patients with cirrhosis of the liver. This appears to be due to a slower rate of glucuronide conjugation in these patients.<sup>37</sup>

#### Distribution

After chloramphenicol has been absorbed, it rapidly diffuses throughout most of the body fluids. The chief factor which limits diffusion throughout the various body fluids appears to be due to protein binding. Thus, the spinal fluid concentration is only 30% to 50% of that in the blood stream. Chloramphenicol appears to diffuse into joint and pleural spaces in somewhat higher concentrations. It penetrates the aqueous and vitreous humor of the eye and crosses the placental barrier. The concentration in the newborn infant's blood is 30% to 80% of that in the maternal blood.<sup>38</sup>

#### THERAPEUTIC INDICATIONS AND CLINICAL USE

Although chloramphenicol is a broad spectrum antibiotic whose effectiveness has been established in a variety of infections due to gram-positive and gram-negative organisms, its toxic effects may be extremely serious and it should not be used when penicillin, the tetracyclines, or erythromycin are effective. This fact reduces the specific indications for the use of this drug to severe salmonella infections, especially typhoid fever. Formerly, chloramphenicol was considered the drug of choice in the treatment of *H influenza* meningitis. A recent comparative study of a large group of patients indicated a mortality rate of 24.5% with oxytetracycline, 8.4% with tetracycline, and 12.5% with chloramphenicol therapy.<sup>39</sup>

Chloramphenicol is highly effective and specific in the treatment of typhoid fever. Bacteremia ceases within a few hours after the first dose. During the next 2 days the patient begins to feel better, although the temperature remains elevated. During the third and fourth day there is dramatic improvement with fall in temperature and disappearance of symptoms. The dose for adults is 2 to 3 gm of chloramphenicol per day administered at 6- or 8-hour intervals. If treatment is discontinued as soon as the patient becomes afebrile, relapse will often occur. This can be prevented in the majority of cases by continuing chloramphenicol for at least 12 days after the afebrile state has been reached.

The effectiveness of chloramphenicol is less dramatic in other salmonella infections and is usually ineffective in eradicating the carrier state.

The development of the newer semisynthetic penicillins may reduce the need for chloramphenicol in the treatment of staphylococcal infections. Probably there are some urinary tract infections in which chloramphenicol is the drug of choice when the organism is resistant to the tetracyclines, erythromycin, and other antibiotics, or to some of the newer antibiotics, such as the colistins, but such instances are uncommon.

There is no justification for employing chloramphenicol prophylactically in surgical patients or in those with salmonella infections or respiratory infections due to viruses.

Chloramphenicol (as well as most antibiotics) has been used far more extensively than the above indications justify, despite repeated warnings in the literature. Several authors have emphasized that fatal reactions have occurred in