widespread oral lesions of the thrush type. Diarrhea and irritation of perianal tissues have been reported after prolonged administration of chloramphenicol and in patients previously treated with the antibiotic. These conditions are usually mild and disappear when chloramphenicol therapy is stopped, although occasionally they are protracted.

The pathogenesis of pseudomembranous enterocolitis of the intestines is not clear, but commonly staphylococci have been implicated. This severe reaction occurs in patients already ill with pneumonia or peritonitis, or it may follow surgical operation. Pseudomembranous enterocolitis has been reported in a few patients receiving chloramphenicol.

Hypersensitivity Reactions

Angioneurotic edema and vesicular and maculopapular types of dermatitis have been reported in patients sensitive to chloramphenicol. Urticaria and vesicular lesions also have been observed. Dermal lesions, usually mild, ordinarily subside promptly when the drug is stopped.

The Jarisch-Herxheimer reaction has been reported after chloramphenicol therapy in patients with syphilis, brucellosis, and typhoid fever. In patients with typhoid fever treated with chloramphenicol, several investigators have recorded a "shock-type reaction" characterized by circulatory collapse, attributed to sudden release of typhoidal endotoxin in an already weakened patient. Unlike the Herxheimer reaction, temperature is usually depressed, but exacerbation of fever has been reported. Recrudescense usually appears within 24 hours of the start of chloramphenicol therapy and persists from 24 to 48 hours.

Neurotoxic Reactions

Headache, mild depression, "dazed feelings," internal ophthalmoplegia, mental confusion, and delirium have been described in patients receiving chloramphenicol for a variety of infectious diseases. Optic and peripheral neuritides as probable effects of prolonged chloramphenicol therapy have been reported. Analysis of these cases suggests that these neurotoxic reactions were related both to large total doses of chloramphenicol and long periods of administration. The range of total dosages of chloramphenicol was from 190 to 1600 Gm. Toxic symptoms appeared between 42 days and 22 months after the start of therapy. Five patients had blurred vision as the most prominent symptom and in a sixth the initial complaint was blindness. This latter was the only one with permanent impairment of vision. Peripheral neuritis resolved in all patients except one, who still had minor residual symptoms thirteen months after onset. If symptoms of decreased visual acuity or peripheral neuritis occur during therapy, prompt withdrawal of the drug is indicated and large doses of oral or parenteral vitamin B complex should be considered.

Other Reactions

The use of this antibiotic, as with other antibiotics, may result in an overgrowth of nonsusceptible organisms, particularly monilia. Constant observation of the patient is essential. If new infections caused by nonsusceptible organisms appear during therapy, appropriate measures should be taken.

CLINICAL USE OF CHLORAMPHENICOL

Rickettsial Diseases

The response of patients with rickettsial infections, including epidemic and murine typhus fevers, Brill's disease, scrub typhus fever, Rocky Mountain spotted fever, and rickettsial pox, has been dramatic with virtual elimination of mortality and marked shortening of the course of illness. Average length of the febrile period after administration of chloramphenicol is 2 days in patients with epidemic typhus fever and 3 days in those with other typhus fevers. Treatment should be given for a minimum of 6 days or 4 days after temperature returns to normal.

Relapse may occur when treatment is given only for 48 hours early in the disease. This can be prevented by giving additional doses on the fifth and sixth days after the initial course. Also, patients in relapse respond as readily to treatment as do those with primary infection.

In patients with Rocky Mountain spotted fever, defervescence occurs about the fourth day after therapy is started. Treatment should be continued for 24 hours after normal temperature is attained.

Typhoid Fever

Chloramphenicol has been established as the drug of choice for this disease. After therapy is started, fever subsides in 3 or 4 days regardless of age, severity of illness, or stage of disease. To lessen possibility of relapse, it is important that therapy be continued for from 8 to 10 days after reaching the afebrile period. Close observation of the patient for complications of the disease, and for aforementioned side effects of the drug, is essential. Results of chloramphenicol treatment for the carrier state are equivocal.

Other Salmonelloses

While chloramphenicol has proved to be a useful therapeutic agent in ameliorating and shortening the clinical course of salmonella infections other than typhoid, results are not as uniform. Recommended duration of treatment is the same as for typhoid fever.

Urinary Tract Infections

Treatment for infections of the urinary tract should be based upon sensitivity of bacteria and on anatomic factors contributing to the infection. The more common organisms encountered in the urinary tract infections are *Esch. coli*, *A. aerogenes*, *Ps. aeruginosa*, *Proteus sp.*, *Staph. aureus* and *Strep. fecalis*.

Chloramphenicol has been found effective in treatment for about 70 per cent of urologic infections, particularly those caused by *Esch. coli*, *Strep. fecalis*, and *Proteus sp.* Relief of symptoms and repeated bacteriological studies should be depended upon to indicate duration of treatment.