GENERIC AND TRADE NAMES OF DRUGS

Chloramphenicol—*Chloromycetin.*
Phenylbutazone—*Butazolidin.*
Testosterone—*Androlin, Andronaq, Andrusol, Malestrone, Mertestate, Neo-Hombreol F, Oreton, Testrandrone, Testosteroid, Testrone, Testryl.*
Prednisone—*Paracortol, Sterane, Sterolone.*
Sulfamethoxyridazine—*Kynex, Midicel.*
Sulfisoxazole—*Gantrisin.*
Acetazolamide—*Diamox.*
Chlorothiazid—*Diuril.*
Chlorpropamide—*Diabinese.*
Tolbutamide—*Orinase.*
Trimethadione—*Tridione.*

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CHLORAMPHENICOL TOXICITY IN LIVER AND RENAL DISEASE

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Erythropoietic depression can be detected in patients receiving chloramphenicol before any noticeable decrease occurs in peripheral blood values. Previous studies,[1,2] have shown that an increase in serum iron content and an increased saturation of iron-binding globulin precedes the fall in hematocrit by an appreciable interval in patients exhibiting toxic effects. These changes have been correlated with prolonged plasma clearance (T/2) of radioactive iron (Fe^{59}), delayed appearance of Fe^{59} in circulating erythrocytes, and decreased marrow uptake of Fe^{59} as detected by external scanning. Utilizing these techniques it has been shown that erythropoietic depression due to chloramphenicol is more frequent than in general realized. Early detection permits discontinuation of the drug before irreversible damage to the hematopoietic system occurs.

The mechanism by which chloramphenicol produces erythropoietic depression is unknown. There is evidence that the nitrobenzene moiety may be important since replacement of the nitro group by a methylmercapto, a methylsulfonyl, or a sulfamoyl group results in increased erythropoietic toxicity.[2-4] Other factors such as the amount and duration of therapy may be factors in producing toaxicity. Kunin, Glazko, and Finland[5] have shown that the half life of chloramphenicol metabolites is increased in severe renal disease and in some patients with hepatic cirrhosis. The possible relationship of these observations to hematologic toxicity was not, however, investigated.

The present study was undertaken to determine whether decreased excretion or impaired conjugation might be factors in producing erythropoietic depression. Accordingly, the incidence of erythropoietic depression was determined in patients with either renal or hepatic insufficiently and correlated with alterations in serum concentration of chloramphenicol metabolites. It was found that there was a marked increase in the incidence of erythropoietic depression in both liver and renal insufficiency and that there was a significant increase in serum concentration of free or active chloramphenicol in all patients developing hematologic toxicity.

MATERIALS AND METHODS

Sixteen patients with hepatic insufficiency due to Laennec's cirrhosis of the liver were studied. The diagnosis was established by clinical findings and confirmed by laboratory evidence of impaired liver function. The ages ranged from 30 to 64 years with a mean age of 42 years. There were six white males, one Negro male, six Negro females, and three white females. Of these 16 patients, two had ascites, three had jaundice, four had both ascites and jaundice, and seven patients had neither ascites nor jaundice.

Nineteen patients with chronic renal insufficiency were also chosen for study. All had hyposthenuria and blood urea nitrogen values of over 22 mg% but less than 70 mg%. All of the patients had chronic pyelonephritis associated with other

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NOTE.—Numbered footnotes at end of article, p. 2706.