HEPATOTOXICITY OF ORAL CONTRACEPTIVES*

Kamal Ishak

Hepatic Pathology Department
Armed Forces Institute of Pathology
Washington, District of Columbia

INTRODUCTION

Hepatic effects of oral contraceptives (OCs) range from multiple biochemical changes\(^1,2\) to structural alterations. The latter can be subcellular or may lead to a variety of diseases that mimic those related to diverse etiologies\(^3,4\). The adverse effects of OCs are most conveniently classified into those affecting the bile excretory system, vessels of the liver or hepatocytes; the latter are mainly hyperplastic and neoplastic processes. Miscellaneous effects of OCs on pre-existing liver disease, as well as the association of these agents with gallstones and pancreatitis, will also be discussed briefly.

INTRAHEPATIC CHOLESTASIS

The syndrome, which develops during the first or second cycle, is ushered in by pruritus, sometimes associated with malaise, anorexia and nausea\(^5-7\). Jaundice follows in one to two weeks. Total serum bilirubin levels are generally below 10 mg/dl. Alkaline phosphatase activity is only slightly or moderately increased and aminotransferase values are generally below 100 IU. Clinical recovery is usually prompt, but several weeks may elapse before all biochemical parameters return to normal. Chronic cholestasis, resembling that occasionally reported with the androgenic anabolic/steroids, does not occur.

Hepatic biopsy specimens obtained during the cholestatic phase reveal cytoplasmic and canalicular cholestasis that predominantly affects acinar zones 3 (Figure 1). There may be evidence of unicellular hepatocytic injury (acidophilic bodies, focal necrosis) and slight hypertrophy of Kupffer cells; portal inflammation is generally absent or very mild. The ultrastructural changes are not helpful in differential diagnosis since they resemble those of cholestasis of other etiologies\(^8,9\).

* The opinions and assertions contained herein are the expressed views of the author and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.
Figure 1. Intrahepatic cholestasis in 21 year old women who had used an oral contraceptive preparation containing norethindrone and mestranol for two weeks. The patient had developed jaundice during the last trimester of a past pregnancy (HE X630).

Figure 2. Sinusoidal dilatation with atrophy of liver cell plates involving acinar zones 1 and 2 (Masson X55).