The World Health Organization lent authority to such apprehension in a port on oral contraceptives about 18 months ago. "There is at present no equate explanation for the oral activity of these compounds or of their fluence on secretion and metabolism. There have been reports of an apparent se in pregnancy rates after cessation of combined treatment, an increase in ucose tolerance (with consequent risks of diabetes mellitus), an increase in agulability of blood, and liver disturbance. All these phenomena need to be vestigated."

SYNTHETICS MORE ACTIVE ORALLY THAN NATURAL AGENTS

Progesterone is weak when taken orally. The ethynyl and other changes at 17, plus removal of the angular methyl between rings A and B, impart oral tivity of progestins. Chlorine or methyl at C-6 also adds to oral potency. sition of norethynodrel's double bond lessens possible androgenic action. Natural estrogens are also weak acting when taken orally. Adding an ethynyl C-17 eases passage of the compound from the intestines into the blood stream, e concept holds, allowing low dosages.

nthetic progesterones

$$\begin{array}{c} \text{OH} \\ \text{OH} \\ \text{C=0 O} \\ \text{C-C-C-OH} \\ \text{O=} \\ \text{C1} \end{array}$$

Norethynodrel

Norethindrone

Chlormadinone acetate

$$\begin{array}{c} CH_3 \\ C=0 \\ O \\ O \\ CH_3-C-O \end{array}$$

$$\begin{array}{c} CH_3 \\ C=0 \\ O \\ CH_3-C-O \end{array}$$

$$\begin{array}{c} CH_3 \\ C=0 \\ O \\ O \\ CH_3-C-O \end{array}$$
Norethindrone acetate
$$\begin{array}{c} CH_3 \\ C=0 \\ O \\ O \\ CH_3-C-O \end{array}$$

Norethindrone acetate

$$CH_3$$
 $C=0$
 $C=0$
 CH_3
 $C=0$
 CH_3
 $CH_$

C = CH $\dot{\mathbf{C}}\mathbf{H}_3$

он

Dimethisterone