

among users, there was a preponderance of hepatic cell adenomas and focal nodular hyperplasia; together, these two types represented 82.6 percent of all benign tumors in users. So it appears that the association between oral contraceptives and benign liver tumors applies only to these two types. The incidence of adenomas peaked significantly in the 26-30 year-old group, and then declined sharply; the incidence of focal nodular hyperplasia peaked in the 31-35 year-olds and then remained rather constant in the older groups.

Editor: *Do the statistics vary with different types of oral contraceptives?*

Dr. Kretzschmar: Two synthetic estrogens are used in oral contraceptives: ethinyl estradiol and mestranol. (Mestranol is demethylated in the liver to ethinyl estradiol.) Where information was available on the type of synthetic estrogen used, 66.7 percent of the tumors were found in women who had used mestranol. But that correlation should be interpreted rather cautiously, since mestranol was marketed first, and until 1970, was used more frequently than ethinyl estradiol by the general population.

Editor: *What were the most common presenting symptoms, and how were these tumors treated?*

Dr. Kretzschmar: Many presented with symptoms of intraperitoneal bleeding, although masses and pain were generally the most frequent presenting symptoms in the survey. It would appear that contraceptive users had highly vascularized tumors, and this might suggest that oral contraceptives exacerbate clinical symptomatology of these tumors. But it should be noted that a high proportion of these benign liver tumors were asymptomatic and were discovered incidentally. I think clinicians should be especially aware of this diagnostic possibility when examining young women who appear otherwise healthy.

Most hepatic cell adenomas studied in this survey were treated by surgical resection, but 13 percent were untreated, and of the cases of focal nodular hyperplasia, 14 percent were untreated. There may be a spontaneous regression of these tumors once oral contraceptive use has been discontinued.

These two types of benign liver tumors have not been shown to be precursors of hepatocellular carcinoma, and there is no evidence that because of different pathogenic mechanisms, the benign tumors in patients on oral contraceptives have any proclivity for malignant degeneration. But benign hepatic lesions can suddenly and unexpectedly rupture, and hemorrhage into the abdominal cavity. Emergency resection of the tumors has not always prevented fatalities. Clinicians should be aware that oral contraceptive users are at risk in relation to these benign liver tumors, and should follow their patients accordingly.

Editor: *Do you recommend the use of DES as a morning-after pill, given its proven correlation with vaginal carcinoma in female*

children of women who received the drug early in pregnancy?

Dr. Kretzschmar: I think that for any patient who is fully aware of the controversies about it, DES is an appropriate management for the morning-after situation, as is menstrual extraction.

Editor: *What are the major contraindications to the use of oral contraceptives?*

Dr. Kretzschmar: Women with present or past thrombophlebitis or thromboembolic disorders should not take the Pill. Similarly, patients with a history of cerebrovascular and coronary artery disease should use another form of contraception. Impaired liver function, known or suspected carcinoma of the breast or estrogen-dependent cancers are other contraindications. The Pill should not be used when pregnancy is suspected, and any undiagnosed abnormal genital bleeding should be investigated and treated before an oral contraceptive is prescribed.

Editor: *In your experience, what is the most common side effect of the Pill, and how should it be treated?*

Dr. Kretzschmar: The most common side effect is breakthrough bleeding, and this should be treated with an increased dosage of estrogen. As a general principle, a patient should begin with the lowest level of estrogen that will prevent ovulation. If breakthrough bleeding persists, the estrogen dosage can be gradually increased. And I'm sure the physician can find another oral contraceptive—assuming the patient is healthy—that will not cause this side effect.

Editor: *Should the Pill be prescribed for uses other than contraception?*

Dr. Kretzschmar: This is done, and I think it's acceptable. For example, it's effective and relatively safe in the management of severe dysmenorrhea.

Oral contraceptives also provide an effective control of prolonged or excessive bleeding. When there is no pathologic basis for the menorrhagia—such as leiomyomas, polyps, and the like—combination agents are very successful in reducing the blood flow. The advantage of this is obvious.

Editor: *To sum up, for whom is it safe to prescribe the Pill?*

Dr. Kretzschmar: A safe candidate for the Pill is any healthy young woman who wishes to have temporary control of her fertility. And I emphasize the word *temporary*. Neither patients nor physicians should avoid the Pill out of fear of carcinogenicity. There is simply no convincing evidence that the Pill causes cancer.

Editor: *Thank you Dr. Kretzschmar*