Citations from the Literature

This is a selection of abstracts taken from the literature in the field of obstetrics and gynecology which the Journal's Editors feel may be of interest to our readers*

**ENDOCRINOLOGY**

Metabolic changes during the normal menstrual cycle: A longitudinal study
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AM J OBSTET GYNECOL 1990, 163/1 II SUPPL (414--416)

The effect of sex hormones on lipid metabolism and coagulation during the menstrual cycle was studied in 37 women. Each woman had three samples drawn, corresponding to the follicular phase, midcycle, and the luteal phase. Basal conditions were obtained by taking samples in the morning while subjects were still in bed. No changes were found in lipids and lipoproteins during the menstrual cycle. Antithrombin III and factor VII of the coagulation system did not change throughout the cycle. Fibrinogen increased in the luteal phase, and all samples of fibrinogen correlated positively with progesterone concentration. This increase, therefore, could be a progesterogenic effect. In conclusion, these findings suggest that when studied optimally no changes in lipids and lipoproteins are found and that the day of blood samples is of minor importance, for instance, when used as a control in studies of oral contraceptives. For investigations on some coagulation parameters, the days of the cycle may be of importance.

Influence of oral contraceptives on coagulation tests in native blood and plasma
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Routine coagulation laboratory tests, clotting times in native (not anticoagulated) whole blood, platelet-rich and platelet-poor plasma, and recalcification times in citrated whole blood, platelet-rich and platelet-poor plasma were performed in 14 healthy premenopausal women. Blood was taken before and after one or two cycles of low-dose oral contraceptives. After oral contraceptives a reduction in clotting time in native platelet-rich plasma and activated partial thromboplastin time were observed. Recalcification times in whole blood and platelet-rich plasma were shorter than clotting times in their native counterparts. The observed changes are compatible with a procoagulant effect seen soon after the start of oral contraceptive use. The absence of these changes in the recalcification times in citrate systems suggests a masking effect of citrate. The reduction in clotting times in native platelet-rich but not in platelet-poor plasma indicates that the hypercoagulability in oral contraceptives users is mainly related to platelets.

Hemostasis profile in women taking low-dose oral contraceptives
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AM J OBSTET GYNECOL 1990, 163/1 II SUPPL (420--423)

Thirty-six young, healthy, nonsmoking women have been selected to check the effect of low-dose oral contraceptives on hemostasis. Two identical groups were treated by Marvelon (a monophasic oral contraceptive containing ethinyl estradiol and desogestrel) or Trigynon (a triphasic oral contraceptive containing ethinyl estradiol and levonorgestrel) for a 6-month period. In the absence, previously controlled, of substantial differences between the effects of each treatment on hemostasis, all the results were pooled at the third and sixth month of the study. The effects of oral contraceptive treatment were as follows: (1) platelet number, platelet aggregating ratio, and plasma α2-thromboglobulin level were not significantly altered, and (2) antithrombin III activity was not reduced despite a slight decrease or antigen concentration. The von Willebrand factor parameters, factor VIII:C, factor VII:C, and clottable fibrinogen were significantly increased. Plasminogen (activity and antigen concentrates) and α2-antiplasmin levels were also significantly increased. Activated partial thromboplastin time and euglobulin lysis time measured after venous occlusion were significantly shortened. Although statistical analysis did not show dramatic changes in all these parameters, some individual extreme values were substantially altered. Therefore we believe that these later values are worthy of cautious consideration for weighing the role that hemostasis factors might play in individual thrombotic risk.

Comparative studies of 30 μg ethinyl estradiol combined with gestodene and desogestrel on blood coagulation, fibrinolysis, and platelets
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AM J OBSTET GYNECOL 1990, 163/1 II SUPPL (430–437)

An association between an increase in the incidence of thromboembolic disease and the use of combined oral contraceptives has been shown by several epidemiologic studies. Evidence of the vascular complications of oral contraceptives suggests that venous thromboembolism correlates with estrogen dosage and arterial complications with both estrogen and progestogen components. In 60 healthy, randomly allocated women, the effects of ethinyl estradiol, 30 μg, combined with gestodene, 75 μg, and desogestrel, 150 μg, on blood coagulation, fibrinolysis, and platelet function were compared. Subjects were studied before oral contraceptive use, at 12, 24, 36, and 48 weeks of treatment, and at 6 and 12 weeks after treatment. Both oral contraceptives affected the hemostatic system, but our results indicate that the ethinyl estradiol/gestodene combination causes changes in the hemostatic system similar to those in the ethinyl estradiol/desogestrel combination. Factors VII and X activity were slightly higher with the ethinyl estradiol/desogestrel combination than with the ethinyl estradiol/gestodene combination, possibly reflecting a greater estrogenic effect.

Enhanced generation and resolution of fibrin in women above the age of 30 years using oral contraceptives low in estrogen
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AM J OBSTET GYNECOL 1990, 163/1 II SUPPL (438–442)

Epidemiologic studies have suggested a relationship between the use of oral contraceptives and mortality from cardiovascular diseases in older women. Therefore we studied generation and resolution of fibrin in 28 healthy women above age 30 years, using oral contraceptives containing 30 to 50 μg of ethinyl estradiol. Thirty healthy nonusers served as control subjects. The oral contraceptive group had increased plasma concentration of thrombin-antithrombin III complexes (p < 0.01), which indicated an enhanced generation of thrombin, increased plasma activity of tissue-type plasminogen activator (p < 0.01), decreased plasma activity of plasminogen activator inhibitor (p < 0.01), and increased plasma concentration of fibrin degradation products (p < 0.04). Interestingly, the ratio of thrombin-antithrombin III complexes/fibrin degradation products did not deviate significantly between groups. Twelve of the 28 women using oral contraceptives were light smokers, that is, less than 15 cigarettes per day. There were no differences in the determined variables between smokers and nonsmokers. Our study suggests that healthy women older than 30 years who use oral contraceptives containing 30 to 50 μg of ethinyl estradiol have an enhanced generation and resolution of fibrin, while the hemostatic balance is unaltered. These findings are unaffected by moderate cigarette smoking.

Effects of newer oral contraceptives on the inhibition of coagulation and fibrinolysis in relation to dosage and type of steroid
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AM J OBSTET GYNECOL 1990, 163/1 II SUPPL (396–403)

Oral contraceptives influence plasma proteins, causing changes in plasma procoagulants and fibrinolytic effectors. Estrogen is thought to be responsible for these changes, whereas progestogens, in particular those with an androgenic effect, may influence the magnitude of the changes. This concept is consistent with epidemiologic studies, suggesting a correlation between estrogen dose and cardiovascular episodes in oral contraceptive users. A delayed resolution of fibrin might contribute to an increased risk caused by decreased coagulation inhibition or fibrinolytic efficacy. Estrogen (30 μg or more) has a dose-dependent effect on clotting factors, including antithrombin III and proteins C and S. The effect of high- and low-dose oral contraceptives containing various progestogens on the fibrinolytic system is less clear. We have found that low-dose oral contraceptives containing levonorgestrel or lynestrenol enhance fibrinolysis, as revealed by an increase in plasminogen (30% to 40%), a decrease in histidine-rich glycoprotein (15% to 26%), an increase in tissue plasminogen activator activity (> 150%), and a decrease in tissue plasminogen activator inhibition (30% to 40%), concomitant with a slight decrease in tissue plasminogen activator antigen level (15% to 20%). New oral contraceptives contain less androgenic progestogens. Preliminary results of an ongoing study of women receiving either 20 μg of ethinyl estradiol with 150 μg of desogestrel or 30 μg of ethinyl plus 75 μg of gestodene revealed no change or changes similar to the older low-dose preparations after 6 months of treatment. Of particular importance was the finding that coagulation activation, expressed by the levels of thrombin-antithrombin III-complexes, fibrin formation, and the efficacy of fibrinolysis, expressed by the levels of fibrin degradation products, was identical in the two groups.

Metabolic changes during treatment with two different progestogens
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AM J OBSTET GYNECOL 1990, 163/1 II SUPPL (374–377)

Two triphasic oral contraceptives containing the same amount of ethinyl estradiol in combination with gestodene or levonorgestrel were compared with respect to contraceptive effect, cycle control, and effects on lipid metabolism and coagulation. Serum concentrations of gestodene, levonorgestrel, ovarian and pituitary hormones, and sex hormone-binding globulin were measured. Thirty-three healthy women were randomized into two groups receiving either of the preparations. Before treatment and in the third and sixth cycles, blood sample were drawn in the morning while subjects were still in bed to obtain basal conditions. The contraceptive effect and cycle control were good with both preparations, and there were only a few minor side effects. Sex hormone-binding globulin was elevated twofold in the levonorgestrel group and threefold in the gestodene group. The gestodene concentration in serum varied more than the levonorgestrel concentration, but with correction for variations in sex hormone-binding globulin binding, less variability in gestodene and levonorgestrel concentrations were seen. High-density lipoprotein cholesterol decreased in the levonorgestrel