

## SCIENCE ABSTRACTS

**Archives of  
Gynecology and Obstetrics**

*S. Fallah et al., Adiponectin, Leptin and Lipid Profiles Evaluation in Oral Contraceptive Pill Consumers, Arch Gynecol Obstet* (December 31, 2011), doi: 10.1007/s00404-011-2192-3 • *Background:* The aim of this study was to evaluate serum lipid profiles, leptin and adiponectin levels in women with a normal menstrual cycle receiving low-dose (LD) combined oral contraceptive pill (COC) (levonorgestrel 0.15 mg, ethinyl-estradiol 0.03 mg). *Study Design:* Serum adiponectin and leptin concentrations were measured by enzyme-linked immunosorbent assay (ELISA), and spectrophotometric assay was used for serum lipid and lipoprotein profiles assay in 50 healthy women with normal menstrual cycles who served as the control group and 50 women taking COCs. Unpaired t test and Chi-square test were used for comparison of variables between oral contraceptive users and non-oral contraceptive users. *Results:* Serum adiponectin and leptin levels were changed in COC consumers. The data obtained for adiponectin in COC consumers ( $6.6 \pm 4.06 \mu\text{g/ml}$ ) were significantly lower (-27.4%,  $P = 0.004$ ) than control group ( $9.1 \pm 5.09 \mu\text{g/ml}$ ). The difference between the serum leptin concentration of the control group ( $11.5 \pm 6.9 \text{ ng/ml}$ ) and women receiving COCs ( $14.1 \pm 6.7 \text{ ng/ml}$ ) was not significant (+18.4%,  $P = 0.083$ ). There was nonsignificant difference between HDL levels of subjects taking COC ( $44.02 \pm 10.7 \text{ mg/dl}$ ) and control group ( $49.4 \pm 14.3 \text{ mg/dl}$ ). The LDL levels of COC consumer ( $131.40 \pm 66.40 \text{ mg/dl}$ ) was significantly higher ( $P = .002$ ) than controls ( $102.30 \pm 44.0 \text{ mg/l}$ ). The serum cholesterol concentration of women receiving COC ( $193.2 \pm 70.4 \text{ mg/dl}$ ) was significantly higher ( $P = 0.05$ ) than controls ( $172.8 \pm 49.6 \text{ mg/dl}$ ). The age of COC consumption and the duration of intake of COCs

beyond 36 months had no significant effect on the adiponectin and leptin concentrations. *Conclusion:* LD COC uptake results in a significant decrease in serum adiponectin concentration, nonsignificant increase in leptin levels and a more atherogenic lipid profile by significantly increasing LDL and nonsignificantly decreasing HDL concentrations. These findings suggested that COC may reduce or stimulate the adiponectin and leptin concentrations, respectively. This might be due to an effect of these pills on adipocyte maturation via inhibition or stimulation of the synthesis of new adiponectin and leptin molecules or may be a result of the increased frequency of a particular allele of the adiponectin and leptin. It is suggested that these alterations in adiponectin and leptin concentrations and lipid profiles may be related to their probable effects in response to various pathological and physiological properties of COC or its metabolites. It seems that probably free radicals produced during metabolism of COCs change the amounts of adipokines and atherogenic lipids.

**BMJ**

*Ø. Lidegaard et al., Risk of Venous Thromboembolism from Use of Oral Contraceptives Containing Different Progestogens and Oestrogen Doses: Danish Cohort Study, 2001–9, BMJ* 343.d6423 (October 25, 2011), doi:10.1136/bmj.d6423 • *Objective:* To assess the risk of venous thromboembolism from use of combined oral contraceptives according to progestogen type and oestrogen dose. *Design:* National historical registry based cohort study. *Settings:* Four registries in Denmark. *Participants:* Non-pregnant Danish women aged 15–49 with no history of thrombotic disease and followed from January 2001 to December 2009. *Main Outcome Measures:* Relative and absolute

risks of first time venous thromboembolism. *Results:* Within 8,010,290 women years of observation, 4307 first ever venous thromboembolic events were recorded and 4246 included, among which 2847 (67%) events were confirmed as certain. Compared with non-users of hormonal contraception, the relative risk of confirmed venous thromboembolism in users of oral contraceptives containing 30 to 40 µg ethinylestradiol with levonorgestrel was 2.9 (95% confidence interval 2.2 to 3.8), with desogestrel was 6.6 (5.6 to 7.8), with gestodene was 6.2 (5.6 to 7.0), and with drospirenone was 6.4 (5.4 to 7.5). With users of oral contraceptives with levonorgestrel as reference and after adjusting for length of use, the rate ratio of confirmed venous thromboembolism for users of oral contraceptives with desogestrel was 2.2 (1.7 to 3.0), with gestodene was 2.1 (1.6 to 2.8), and with drospirenone was 2.1 (1.6 to 2.8). The risk of confirmed venous thromboembolism was not increased with use of progestogen only pills or hormone releasing intrauterine devices. If oral contraceptives with desogestrel, gestodene, or drospirenone are anticipated to increase the risk of venous thromboembolism sixfold and those with levonorgestrel threefold, and the absolute risk of venous thromboembolism in current users of the former group is on average 10 per 10,000 women years, then 2000 women would need to shift from using oral contraceptives with desogestrel, gestodene, or drospirenone to those with levonorgestrel to prevent one event of venous thromboembolism in one year. *Conclusion:* After adjustment for length of use, users of oral contraceptives with desogestrel, gestodene, or drospirenone were at least at twice the risk of venous thromboembolism compared with users of oral contraceptives with levonorgestrel.

### BMJ Open

*D. Margel and N. E. Fleshner, Oral Contraceptive Use Is Associated with Prostate Cancer: An Ecological Study, BMJ Open* (2011), doi: 10.1136/bmjopen-2011-000311 • *Background:* Several recent studies have suggested that oestrogen exposure may increase the risk of prostate cancer

(PCa). *Objectives:* To examine associations between PCa incidence and mortality and population-based use of oral contraceptives (OCs). It was hypothesised that OC by-products may cause environmental contamination, leading to an increased low level oestrogen exposure and therefore higher PCa incidence and mortality. *Methods:* The hypothesis was tested in an ecological study. Data from the International Agency for Research on Cancer were used to retrieve age-standardised rates of prostate cancer in 2007, and data from the United Nations World Contraceptive Use 2007 report were used to retrieve data on contraceptive use. A Pearson correlation and multivariable linear regression were used to associate the percentage of women using OCs, intrauterine devices, condoms or vaginal barriers to the age standardised prostate cancer incidence and mortality. These analyses were performed by individual nations and by continents worldwide. *Results:* OC use was significantly associated with prostate cancer incidence and mortality in the individual nations worldwide ( $r=0.61$  and  $r=0.53$ , respectively;  $p<0.05$  for all). PCa incidence was also associated with OC use in Europe ( $r=0.545$ ,  $p<0.05$ ) and by continent ( $r=0.522$ ,  $p<0.05$ ). All other forms of contraceptives (ie, intra-uterine devices, condoms or vaginal barriers) were not correlated with prostate cancer incidence or mortality. On multivariable analysis the correlation with OC was independent of a nation's wealth. *Conclusion:* A significant association between OCs and PCa has been shown. It is hypothesised that the OC effect may be mediated through environmental oestrogen levels; this novel concept is worth further investigation.

### Cell Reports

*F. Hammachi et al., Transcriptional Activation by Oct4 Is Sufficient for the Maintenance and Induction of Pluripotency, Cell Reports* 1.2 (February 23, 2012): 99–109 • Oct4 is an essential regulator of pluripotency in vivo and in vitro in embryonic stem cells, as well as a key mediator of the reprogramming of somatic cells into induced pluripotent stem cells. It is not

known whether activation and/or repression of specific genes by Oct4 is relevant to these functions. Here, we show that fusion proteins containing the coding sequence of Oct4 or Xlpou91 (the *Xenopus* homolog of Oct4) fused to activating regions, but not those fused to repressing regions, behave as Oct4, suppressing differentiation and promoting maintenance of undifferentiated phenotypes *in vivo* and *in vitro*. An Oct4 activation domain fusion supported embryonic stem cell self-renewal *in vitro* at lower concentrations than that required for Oct4 while alleviating the ordinary requirement for the cytokine LIF. At still lower levels of the fusion, LIF dependence was restored. We conclude that the necessary and sufficient function of Oct4 in promoting pluripotency is to activate specific target genes.

### Cell Stem Cell

*M. Choudhary et al., Egg Sharing for Research: A Successful Outcome for Patients and Researchers, Cell Stem Cell* 10.3 (March 2, 2012): 239–240 • Recent discussions in this journal have identified the research need for donated eggs, concern for the welfare of the donor, and the ongoing ethical debate about financial compensation. It is generally acknowledged that there needs to be robust regulatory oversight that takes into account the physical risks incurred by the donor. In response to these issues, we initiated an egg-sharing scheme for women undergoing IVF treatment. Review of the outcome for these women indicates that this source of eggs has proved to be successful for both patients and researchers.

### Clinical and Experimental Obstetrics and Gynecology

*G. Iatrakis et al., The Role of Oral Contraceptive Use in the Occurrence of Breast Cancer: A Retrospective Study of 405 Patients, Clin Exp Obstet Gynecol* 38.3 (2011): 225–227 • The investigation of potential predisposing factors of breast cancer, a disease accounting for almost one-third of malignancies in women, is necessary in order to reduce the incidence. *Materials and Methods:* We interviewed

405 female patients who had been diagnosed with breast cancer and who also reported having used oral contraceptive pills before. They were categorized into two groups (group A <7 years OC use and group B >7 years OC use). *Results:* Statistical analysis revealed a small ( $p < 0.02$ ) but significant increased risk of the disease to BRCA mutation carriers, as well as to the women with a significant medical or family history of breast, ovarian or colon cancer who had also previously used oral contraceptive pills for more than seven years. *Discussion:* Breast cancer seems to be positively dependent on prolonged oral contraceptive use. *Conclusion:* More research is needed to establish the hypothesis that the human genome is vulnerable to oral contraceptives.

### European Journal of Contraception and Reproductive Health Care

*F. Martinez et al., Venous and Pulmonary Thromboembolism and Combined Hormonal Contraceptives: Systematic Review and Meta-analysis, Eur J Contracept Reprod Health Care* 17.1 (February 2012): 7–29 • *Objective:* A systematic review of studies published between January 1995 and April 2010 aimed at determining the effect of combined hormonal contraceptives (CHCs), administered orally, transdermally or vaginally, on the risk of venous thromboembolism (VTE). *Results:* Of the 625 potentially eligible references reviewed, 25 studies meeting the inclusion and exclusion criteria were entered in the meta-analysis. The pooled relative risks of VTE associated with the various CHCs, depending on their progestogen, were: gestodene vs. levonorgestrel 1.33 (95% confidence interval [CI]: 1.08–1.63); desogestrel vs. levonorgestrel 1.93 (95% CI: 1.31–2.83); and drospirenone vs. levonorgestrel 1.67 (95% CI: 1.10–2.55). The pooled adjusted odds ratio for norgestimate vs. levonorgestrel was 1.11 (95% CI: 0.84–1.46) and that for cyproterone acetate vs. levonorgestrel 1.65 (95% CI: 1.30–2.11). *Conclusions:* The safest CHCs in terms of VTE are those containing levonorgestrel or norgestimate. The risk of VTE associated

with desogestrel-, drospirenone- or cyproterone acetate-containing CHCs is greater than that associated with CHCs containing levonorgestrel. The increased risk of VTE found for CHCs with gestodene compared to CHCs with levonorgestrel seems smaller than in previous analyses. There were no differences in VTE risk between oral and transdermal CHCs containing norgestimate or norelgestromin, respectively.

### Evolution and Human Behavior

*C. Athena Aktipis, Is Cooperation Viable in Mobile Organisms? Simple Walk Away Rule Favors the Evolution of Cooperation in Groups, *Evol Hum Behav* 32.4 (July 2011): 263–276* • The evolution of cooperation through partner choice mechanisms is often thought to involve relatively complex cognitive abilities. Using agent-based simulations, I model a simple partner choice rule, the “Walk Away” rule, where individuals stay in groups that provide higher returns (by virtue of having more cooperators), and “Walk Away” from groups providing low returns. Implementing this conditional movement rule in a public goods game leads to a number of interesting findings: (a) cooperators have a selective advantage when thresholds are high, corresponding to low tolerance for defectors, (b) high thresholds lead to high initial rates of movement and low final rates of movement (after selection), and (c) as cooperation is selected, the population undergoes a spatial transition from high migration (and many small and ephemeral groups) to low migration (and large and stable groups). These results suggest that the very simple “Walk Away” rule of leaving uncooperative groups can favor the evolution of cooperation and that cooperation can evolve in populations in which individuals are able to move in response to local social conditions. A diverse array of organisms are able to leave degraded physical or social environments. The ubiquitous nature of conditional movement suggests that “Walk Away” dynamics may play an important role in the evolution of social behavior in both cognitively complex and cognitively simple organisms.

*R. B. Bird et al., The Hierarchy of Virtue: Mutualism, Altruism and Signaling in Martu Women’s Cooperative Hunting, *Evol Hum Behav* 33.1 (January 2012): 64–78* • Cooperative hunting is often assumed to be mutualistic, maintained through returns to scale, where, by working together, foragers can gain higher per capita return rates or harvest sizes than they can by hunting alone. We test this hypothesis among Martu hunters and find that cooperation only provides increased returns to poorer hunters while disadvantaging better hunters. Even so, better hunters still cooperate as frequently as poorer hunters. We ask whether better hunters are advantaged in secondary sharing distributions or whether they bias their partner choice to kin or household members. We find that better hunters are not more likely to pair up with kin and they do not gain consumption benefits from acquiring more. They share a greater proportion of their harvest than poorer hunters: no matter how much one produces—better hunter, worse hunter, cooperator, solitary hunter—all eat the same amount in the end. Such a result suggests the hypothesis that cooperation might be a costly signal of commitment to the public interest on the part of better hunters, which generates trust among camp members and facilitates strong social networks, particularly among women, who cooperate more than men. While some foragers may benefit through cooperation from returns to scale or risk reduction, others may benefit more through signaling commitment and generating trust.

*P. DeScioli et al., The Omission Effect in Moral Cognition: Toward a Functional Explanation, *Evol Hum Behav* 32.3 (May 2011): 204–215* • Moral judgment involves much more than computations of the expected consequences of behavior. A prime example of the complexity of moral thinking is the frequently replicated finding that violations by omission are judged less morally wrong than violations by commission, holding intentions constant. Here we test a novel hypothesis: Omissions are judged less harshly because they produce little material evidence of wrongdoing. Evidence is crucial

because moral accusations are potentially very costly unless supported by others. In our experiments, the omission effect was eliminated when physical evidence showed that an omission was chosen. Perpetrators who “opted out” by pressing a button that would clearly have no causal effects on the victim, rather than rescuing them, were judged as harshly as perpetrators who directly caused death. These results show that, to reduce condemnation, omissions must not only be noncausal, they must also leave little or no material evidence that a choice was made.

*D. B. Krupp et al.*, **Apparent Health Encourages Reciprocity**, *Evol Hum Behav* 32.3 (May 2011): 198–203 • Reciprocity evolves only when social partners reliably repay, with interest, the investments of others. However, not all individuals are equally able—or motivated—to recompense others satisfactorily. As such, reciprocity relies greatly on the capacities and motives of partners. Apparent health may provide a cue to the value of potential exchange partners in this regard: healthier individuals will tend to live longer and accrue more, higher quality resources, thus increasing the incentives for mutual cooperation. In a monetary exchange task, we show that the apparent health of partners’ faces affects human reciprocity. Specifically, participants were more willing to return a profitable amount to, but not more willing to invest in, apparently healthy than unhealthy partners. This effect appears to be a function of the attractiveness of apparent health, suggesting a preference for repayment of attractive partners. Furthermore, the effect of apparent health on reciprocal exchange is qualified by the sex of the partners, implicating a history of sexual selection in the evolution of human social exchange.

### Human Molecular Genetics

*S. V. Diaz Perez et al.*, **Derivation of New Human Embryonic Stem Cell Lines Reveals Rapid Epigenetic Progression In Vitro that Can Be Prevented by Chemical Modification of Chromatin**, *Hum Mol Genet* 21.4 (February 15, 2012): 751–764 • Human embryonic stem cells (hESCs) are pluripotent

cell types derived from the inner cell mass of human blastocysts. Recent data indicate that the majority of established female XX hESC lines have undergone X chromosome inactivation (XCI) prior to differentiation, and XCI of hESCs can be either XIST-dependent (class II) or XIST-independent (class III). XCI of female hESCs precludes the use of XX hESCs as a cell-based model for examining mechanisms of XCI, and will be a challenge for studying X-linked diseases unless strategies are developed to reactivate the inactive X. In order to recover nuclei with two active X chromosomes (class I), we developed a reprogramming strategy by supplementing hESC media with the small molecules sodium butyrate and 3-deazaneplanocin A (DZNep). Our data demonstrate that successful reprogramming can occur from the XIST-dependent class II nuclear state but not class III nuclear state. To determine whether these small molecules prevent XCI, we derived six new hESC lines under normoxic conditions (UCLA1-UCLA6). We show that class I nuclei are present within the first 20 passages of hESC derivation prior to cryopreservation, and that supplementation with either sodium butyrate or DZNep preserve class I nuclei in the self-renewing state. Together, our data demonstrate that self-renewal and survival of class I nuclei are compatible with normoxic hESC derivation, and that chemical supplementation after derivation provides a strategy to prevent epigenetic progression and retain nuclei with two active X chromosomes in the self-renewing state.

### Lancet Infectious Diseases

*R. Heffron et al.*, **Use of Hormonal Contraceptives and Risk of HIV-1 Transmission: A Prospective Cohort Study**, *Lancet Infect Dis* 12.1 (January 2012): 19–26 • *Background*: Hormonal contraceptives are used widely but their effects on HIV-1 risk are unclear. We aimed to assess the association between hormonal contraceptive use and risk of HIV-1 acquisition by women and HIV-1 transmission from HIV-1-infected women to their male partners. *Methods*: In this prospective study, we followed up 3790

heterosexual HIV-1-serodiscordant couples participating in two longitudinal studies of HIV-1 incidence in seven African countries. Among injectable and oral hormonal contraceptive users and non-users, we compared rates of HIV-1 acquisition by women and HIV-1 transmission from women to men. The primary outcome measure was HIV-1 seroconversion. We used Cox proportional hazards regression and marginal structural modeling to assess the effect of contraceptive use on HIV-1 risk. *Findings:* Among 1314 couples in which the HIV-1-seronegative partner was female (median follow-up 18.0 [IQR 12.6–24.2] months), rates of HIV-1 acquisition were 6.61 per 100 person-years in women who used hormonal contraception and 3.78 per 100 person-years in those who did not (adjusted hazard ratio 1.98, 95% CI 1.06–3.68,  $p=0.03$ ). Among 2476 couples in which the HIV-1-seronegative partner was male (median follow-up 18.7 [IQR 12.8–24.2] months), rates of HIV-1 transmission from women to men were 2.61 per 100 person-years in couples in which women used hormonal contraception and 1.51 per 100 person-years in couples in which women did not use hormonal contraception (adjusted hazard ratio 1.97, 95% CI 1.12–3.45,  $p=0.02$ ). Marginal structural model analyses generated much the same results to the Cox proportional hazards regression. *Interpretation:* Women should be counseled about potentially increased risk of HIV-1 acquisition and transmission with hormonal contraception, especially injectable methods, and about the importance of dual protection with condoms to decrease HIV-1 risk. Non-hormonal or low-dose hormonal contraceptive methods should be considered for women with or at-risk for HIV-1.

### Nature Biotechnology

*T. O'Leary et al., Tracking the Progression of the Human Inner Cell Mass during Embryonic Stem Cell Derivation, Nat Biotech* 30.3 (March 2012): 278–282 • The different pluripotent states of mouse embryonic stem cells (ESCs) *in vitro* have been shown to correspond to stages of mouse embryonic development. For human cells,

little is known about the events that precede the generation of ESCs or whether they correlate with *in vivo* developmental stages. Here we investigate the cellular and molecular changes that occur during the transition from the human inner cell mass (ICM) to ESCs *in vitro*. We demonstrate that human ESCs originate from a post-ICM intermediate (PICMI), a transient epiblast-like structure that has undergone X-inactivation in female cells and is both necessary and sufficient for ESC derivation. The PICMI is the result of progressive and defined ICM organization *in vitro* and has a distinct state of cell signaling. The PICMI can be cryopreserved without compromising ESC derivation capacity. As a closer progenitor of ESCs than the ICM, the PICMI provides insight into the pluripotent state of human stem cells.

### PNAS: Proceedings of the National Academy of Sciences USA

*A. Y. Hoekstra and M. M. Mekonnen, The Water Footprint of Humanity, Proc Nat Acad Sci USA* 109.9 (February 28, 2012): 3232–3237 • This study quantifies and maps the water footprint (WF) of humanity at a high spatial resolution. It reports on consumptive use of rainwater (green WF) and ground and surface water (blue WF) and volumes of water polluted (gray WF). Water footprints are estimated per nation from both a production and consumption perspective. International virtual water flows are estimated based on trade in agricultural and industrial commodities. The global annual average WF in the period 1996–2005 was 9,087 Gm<sup>3</sup>/y (74% green, 11% blue, 15% gray). Agricultural production contributes 92%. About one-fifth of the global WF relates to production for export. The total volume of international virtual water flows related to trade in agricultural and industrial products was 2,320 Gm<sup>3</sup>/y (68% green, 13% blue, 19% gray). The WF of the global average consumer was 1,385 m<sup>3</sup>/y. The average consumer in the United States has a WF of 2,842 m<sup>3</sup>/y, whereas the average citizens in China and India have WFs of 1,071 and 1,089 m<sup>3</sup>/y, respectively. Consumption of

cereal products gives the largest contribution to the WF of the average consumer (27%), followed by meat (22%) and milk products (7%). The volume and pattern of consumption and the WF per ton of product of the products consumed are the main factors determining the WF of a consumer. The study illustrates the global dimension of water consumption and pollution by showing that several countries heavily rely on foreign water resources and that many countries have significant impacts on water consumption and pollution elsewhere.

*M.H. Teicher et al., Childhood Maltreatment Is Associated with Reduced Volume in the Hippocampal Subfields CA3, Dentate Gyrus, and Subiculum, Proc Nat Acad Sci USA 109.9 (February 28, 2012): E563–E572, doi:10.1073/pnas.1115396109 • Childhood maltreatment or abuse is a major risk factor for mood, anxiety, substance abuse, psychotic, and personality disorders, and it is associated with reduced adult hippocampal volume, particularly on the left side. Translational studies show that the key consequences of stress exposure on the hippocampus are suppression of neurogenesis in the dentate gyrus (DG) and dendritic remodeling in the cornu ammonis (CA), particularly the CA3 subfield. The hypothesis that maltreatment is associated with volume reductions in 3-T MRI subfields containing the DG and CA3 was assessed and made practical by newly released automatic segmentation routines for FreeSurfer. The sample consisted of 193 unmedicated right-handed subjects (38% male,  $21.9 \pm 2.1$  y of age) selected from the community. Maltreatment was quantified using the Adverse Childhood Experience study and Childhood Trauma Questionnaire scores. The strongest associations between maltreatment and volume were observed in the left CA2-CA3 and CA4-DG subfields, and were not mediated by histories of major depression or posttraumatic stress disorder. Comparing subjects with high vs. low scores on the Childhood Trauma Questionnaire and Adverse Childhood Experience study showed an average volume reduction of 6.3% and 6.1% in the left CA2-CA3 and CA4-DG, respectively. Volume reductions*

in the CA1 and fimbria were 44% and 60% smaller than in the CA2-CA3. Interestingly, maltreatment was associated with 4.2% and 4.3% reductions in the left presubiculum and subiculum, respectively. These findings support the hypothesis that exposure to early stress in humans, as in other animals, affects hippocampal subfield development.

### Thrombosis Research

*K. Bremme et al., The APC-PCI Concentration as an Early Marker of Activation of Blood Coagulation: A Study of Women on Combined Oral Contraceptives, Thromb Res (December 9, 2011), doi:10.1016/j.thromres.2011.11.006 • Background: The risk of venous thromboembolism (VTE) in women taking combined oral contraceptives (COCs) is attributed to changes in coagulation and fibrinolysis. The impact of the COCs may be greater in women with preexisting thrombophilic defects. Nevertheless most women who suffer from venous thrombosis do not have any of the well known hereditary or acquired risk factors. A simple and sensitive marker of “thrombogenicity” has not been identified. Objectives: To investigate the effects of two different monophasic combined oral contraceptives (COCs) on the plasma concentrations of activated protein C-inhibitor of protein C (APC-PCI) and on comparable hemostatic factors in fertile women. Method: Forty-four healthy nulliparous women with regular menstrual periods were included and randomly assigned to start with a monophasic preparation containing 30µg ethinylestradiol and 150µg levonogestrel (LNG/EE) or a preparation containing 30µg ethinylestradiol and 150 µg desogestrel (DG/EE). After a wash-out period of two months, treatment with the alternate preparation was initiated and continued for two more cycles. Results: The plasma concentration of the APC-PCI complex and thrombin-anti-thrombin complex (TAT) increased during treatment with the two COCs. During DG/EE treatment the APC-PCI complex increased significantly more than during LNG/EE ( $p < 0.01$ ). The plasma concentration of D-dimer did not increase during OC treatment. Conclusion: The APC-PCI complex*

concentration, which serves as a marker for thrombin generation and indicates hypercoagulability, was increased during COC treatment compared to baseline. The method is a sufficiently sensitive marker to detect even small differences in the activation of coagulation.

### **West Indian Medical Journal**

*O. Akinloye et al., Effects of Contraceptives on Serum Trace Elements, Calcium and Phosphorus Levels, West Indian Med 60.3 (June 2011): 308–315 • Background:* Women on different contraceptive methods have been linked with the development of various diseases and possible changes in serum trace elements and vitamins of women on contraceptives have been postulated. Therefore, the relationship between contraceptive use and trace elements needs to be investigated. *Methods:* This is a cross-sectional randomized study. After informed consent was obtained, blood samples were collected from a total of 100 women of child-bearing age on different contraceptive methods: 50 on oral contraceptives, 25 on injectables and another 25 on intra-uterine devices. Blood samples were also collected from another 50 age-matched

non-contraceptive users to serve as control. Serum was analysed using atomic absorption spectrophotometer for zinc, copper manganese, iron, selenium, cadmium, lead and magnesium while colorimetric method was used for phosphorus and calcium. Body mass index (BMI) was calculated as weight in kilogram/height in meter squared. Results obtained from laboratory analysis and anthropometric measurements were analysed using computer SPSS package. *Results:* The mean serum zinc, selenium, phosphorus and magnesium levels obtained from subjects on contraceptives were significantly lower ( $p < 0.01$ ,  $p < 0.05$ ,  $p < 0.05$  and  $p < 0.05$  respectively) than those of the control group. However, the mean serum copper iron, calcium and cadmium levels were significantly higher ( $p < 0.05$ ) in participants on contraceptive when compared with the control group. Manganese and lead levels were similar in participants and control groups. Correlation analysis shows significant association between some trace elements and the duration of contraception and body mass index of the participants. *Conclusion:* The study showed and confirmed reduced levels of trace elements in women on contraceptives. The reduction is proportional to the duration of contraceptive use.