

EDITORIAL

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From the Editor: On Women's Health Del Editor sobre la Salud de la Mujer

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Research on women's health results in thousands of papers published in an infinite number of medical journals. It is not possible to read all this new literature and not all papers are open-access. In this section, we try to summarize some of this investigation, knowledge that we may apply in our daily labor.

IMMUNIZATIONS AND WOMEN

Physicians are not always prepared to assist patients regarding immunizations during the various stages of life. The USA Center for Disease Control and Prevention has published two articles and corresponding tables that summarize immunization schedules recommended to children and adolescents 18 years old or younger, United States, 2019⁽¹⁾, and for adults 19 years old or above, United States, 2019⁽²⁾. We highly recommend reviewing these articles, the tables and recent information on immunizations, since gynecologists and obstetricians should be able to answer questions on the subject to our worried patients. ACOG has also collaborated with the Centers for Disease Control and Prevention (CDC) on a provider resource: Summary of Maternal Immunization Recommendations. This quick reference for providers can be read in the ACOG "Committee Opinion 741. Maternal Immunization"⁽³⁾.

The FDA approved the use of the 9-valent HPV vaccine in women and men aged 27 through 45 years. Although this approval opens the possibility for expanded protection against HPV-related disease in women and men, further review of the available data, including cost-effectiveness, is needed. The decision to be vaccinated among people within this age range should be individually based while considering the patients' circumstances, preferences, and concerns⁽⁴⁾.

It is satisfactory to know that, from 2008–2014, in 10 206 cases in the United States of America, the proportion of HPV16/18-positive CIN2+ has declined, with the greatest declines in vaccinated women; declines in unvaccinated women suggest herd protection⁽⁵⁾.

PRESERVING THE HEALTH OF MOTHERS AND NEWBORNS

Thrombocytopenia, defined as a platelet count of less than $150 \times 10^9/L$, is common and occurs in 7–12% of pregnancies at the time of delivery. Thrombocytopenia can result from a variety of physiologic or pathologic conditions, several of which are unique to pregnancy. Some causes of thrombocytopenia are serious medical disorders that have the potential for maternal and fetal morbidity. In contrast, other conditions, such as gestational thrombocytopenia, are benign and pose no maternal or fetal risks⁽⁶⁾.

Cesarean surgical site infections are frequent in some localities. After implementing a resident-driven quality initiative using a surgical bundle,



a significant decrease in cesarean surgical site infections was observed (2.2% [33/1,523] vs 4.5% [73/1,624]; odds ratio [OR] 0.47 [95% CI 0.31–0.71]; $P < .001$). Interventions that were common but were not standardized before the surgical bundle included use of clippers instead of a razor for hair removal, suture closure of subcutaneous tissue if wound thickness exceeded 2 cm, and dressing removal between 24 and 48 hours. Preoperative azithromycin to all patients undergoing cesarean delivery was implemented before skin incision, as well as postpartum 2% chlorhexidine gluconate showers daily for 7 days⁽⁷⁾.

Investigators had previously found that formerly pre-eclamptic women had cerebral white matter lesions (WMLs) significantly more often (37%) and more severely than controls. Current hypertension and a history of early-onset pre-eclampsia (<37 weeks) were independently associated with the presence of WMLs⁽⁸⁾. Now, a study has found that “true” lacunar infarctions due to hypertensive small vessel disease (lipohyalinosis and fibrinoid necrosis) occur at the base of the brain in a distribution known as the “vascular centrencephalon”. In this distribution, short small arteries with few branches transmit pressure from large arteries to small arterioles. So hypertensive lacunar infarctions and intracerebral hemorrhages are found in the distribution of the basal ganglia, internal capsule, thalamus, and brainstem⁽⁹⁾.

Because the interpregnancy period is a continuum for overall health and wellness, all women of reproductive age who have been pregnant should receive interpregnancy care as a continuation of postpartum care, regardless of the outcome of their pregnancies (ie, miscarriage, abortion, preterm, full-term delivery). This interpregnancy care should include reproductive life planning, screening for depression, vaccination, managing diabetes or hypertension if needed, education about future health, and, in women with chronic medical conditions, making plans for long-term medical care⁽¹⁰⁾.

It is worrisome that approximately 800 women in the US die each year during pregnancy and the postpartum period. The estimated maternal mortality rate was 26.4 deaths per 100 000 live births in 2015. Leading underlying causes were hemorrhage 14% (70% preventable), cardiovascular and coronary conditions 14% (68%

preventable), infection 10.7, cardiomyopathy 10.7%, embolism 8.4%, preeclampsia and eclampsia 7.4%, mental health conditions 7%. All developed countries did better: 4.4 per 100 000 live births in Sweden, 9.2 in the United Kingdom, and 7.3 in Canada. According to international groups, maternal mortality rates dropped by an estimated 44% worldwide from 1990 to 2015—a decline of 48% for industrialized countries. Based on US statistics, pregnancy-related deaths rose there by an estimated 27% from 2000 to 2014⁽¹¹⁾. Medical errors, ineffective treatments, and lack of care coordination by clinicians and hospitals are major causes of preventable death, according to this report. We should add integral education, quality of services and access and transportation as important causes in Latin America.

Given that assisted reproductive technologies continue as the main treatment choice for infertility, we should have in mind new findings from Canada: women who undergo fertility treatments, particularly in vitro fertilization, are at a slightly higher risk of severe maternal morbidity or death. Efforts are needed to identify patient- and treatment-specific predictors of severe maternal morbidity that may influence the type of treatment a woman is offered⁽¹²⁾. Furthermore, children conceived by medically assisted reproduction face an elevated risk of adverse birth outcomes (e.g., difference in birthweight of –60 g (95% CI –86 to –34) and 2.15 percentage point increased risk of preterm delivery (95% CI 1.07 to 3.24). However, results indicate that this increased risk is largely attributable to factors other than the medically assisted reproduction treatment itself⁽¹³⁾.

THE NEWBORN

There is an important message for obstetricians regarding anemia in small infants in Latin America and developing countries. At 4 months, infants born at term who had received delayed umbilical cord clamping (DCC, >5 minutes) had greater ferritin levels and increased brain myelin in areas important for early life functional development. Endowment of iron-rich red blood cells through DCC may offer a longitudinal advantage for early white matter development⁽¹⁴⁾.

A total of 28 628 (1.4%) from 2 050 491 Swedish children presented at least 1 congenital heart defect. Proportional reporting ratios of aortic



arch defects increased with maternal obesity severity. Compared with offspring of normal weight mothers, adjusted prevalence rate ratios of aortic arch defects and transposition of the great arteries were doubled in offspring of mothers with severe obesity⁽¹⁵⁾. The risk of major congenital malformations during the first year of life increases with the mother's weight, from 5% higher in women who are overweight to 37% higher in women with extreme obesity⁽¹⁶⁾. This is an important finding to consider as obesity rates continue to rise.

The BabySeq Project is a pilot trial that explores the medical, behavioral, and economic impact of newborn genomic sequencing (nGS) in healthy newborns and those admitted to a neonatal intensive care unit (NICU) in hospitals in Boston, Massachusetts. nGS revealed a risk of childhood-onset disease in 15/159 (9.4%) newborns; none of the disease risks were anticipated based on the infants' known clinical or family histories; the interpretation of results can substantially benefit from parental testing⁽¹⁷⁾.

Can the mental health of the newborn be influenced by medical incidents during pregnancy or shortly after being born? The Stress in Pregnancy (SIP) Study cohort was set up in New York City in 2009 through funding made available by the National Institute of Mental Health (NIMH) to address this question. Based on the 'Developmental Origins of Health and Diseases (DoHaD) Hypothesis', it seeks to understand the extent to which an adverse environment in utero can alter fetal growth and development, with potential lifelong impacts on health and disease. Growing evidence suggests that not only the genome, but also the epigenome, the heritable, quasi-stable yet dynamic control of gene expression, can be modulated by the environment, and plays a vital role in defining health and disease in growing offspring. Antenatal exposure to broadly defined stress, as well as growth-related suboptimal reproductive outcomes such as intra-uterine growth restriction (IUGR) and obesity, is linked to long-term neurobehavioral problems in offspring, such as autism, schizophrenia and attention deficit/hyperactivity disorder, through epigenetic mechanisms⁽¹⁸⁾.

Furthermore, fetal exposure to a maternal infection while hospitalized appears to increase the risk for autism and depression, but not for

bipolar disease nor psychosis, during the child's life. These results emphasize the importance of avoiding infections during pregnancy, which may impart subtle fetal brain injuries contributing to development of autism and depression⁽¹⁹⁾. The new findings are consistent with other epidemiologic and animal studies which suggest that inflammation during gestation alters brain architecture or transcriptional programs and point to an important possible biological basis for a fetal origin for depression and suicide⁽²⁰⁾.

Maternal social relationships are associated with cognitive development in children, and social relationships beyond the mother-child-father triad are significantly associated with children's cognitive development⁽²¹⁾.

CONCERN ON MENOPAUSAL WOMEN

A probable increased risk of earlier ovarian failure as a possible consequence of premenopausal hysterectomy has been previously reported⁽²²⁾. Now, the occurrence of osteoporosis has been found increased in patients who had undergone hysterectomy compared to that in matched control subjects regardless of bilateral oophorectomy (BO) status. The adjusted HRs for osteoporosis according to hysterectomy/oophorectomy status were 1.43 (95% CI = 1.34-1.51) in the hysterectomy without BO group and 1.57 (95% CI = 1.37-1.79) in the hysterectomy with BO group⁽²³⁾. These findings suggest the need to preserve the uterus in women in reproductive age to avoid consequences in the female hormone physiology.

Men and women have been advised on the consequences of ingesting hypercaloric foods and beverages. Higher intake of artificially sweetened beverages has been associated with increased risk of stroke, particularly small artery occlusion subtype, coronary heart disease, and all-cause mortality⁽²⁴⁾. Also, bone mineral density and coronary calcification are inversely related in both men and postmenopausal women, supporting the hypothesis that a direct relation between bone loss and development of atherosclerosis exists irrespective of gender⁽²⁵⁾.

Regarding dementia and systemic hormone therapy, all postmenopausal women (n=84 739) in Finland who, between 1999 and 2013, received a diagnosis of Alzheimer's disease



from a neurologist or geriatrician, and who were identified from a national drug register, were compared with control women without such diagnosis (n=84 739). In 83 688 (98.8%) women, a diagnosis for Alzheimer's disease was made at the age of 60 years or older, and 47 239 (55.7%) women had been over 80 years old at diagnosis. Use of systemic hormone therapy was associated with a 9-17% increased risk of Alzheimer's disease. The risk of the disease did not differ significantly between users of estradiol only (odds ratio 1.09, 95% confidence interval 1.05 to 1.14) and those of estrogen-progestogen (1.17, 1.13 to 1.21). The higher risk in users of estrogen-progestogen therapy was not related to different progestogens (norethisterone acetate, medroxyprogesterone acetate, or other progestogens). In contrast, use of vaginal estradiol showed no such risk⁽²⁶⁾. Overall, systemic estrogen-progestogen or estradiol-only HT were associated with a small increase in Alzheimer's risk, but for women who began treatment before age 60; a significant risk increase was limited to ten or more years of use⁽²⁷⁾.

CANCER IN WOMEN

A review by Randall et al. addressing thermal ablation in the management of preinvasive cervical lesions considered 34 total reports and 23 meta-analyses that included 10 995 and 6 371 patients respectively, seven studies of which took place in low or middle-income countries (LMICs). The overall response rate for thermal ablation (TA) treatment of biopsy-proven cervical intraepithelial neoplasia grade 2 or higher (CIN2+) was 93.8%. Consistent with the wide variety of settings and patient populations, there was significant heterogeneity between studies. TA appears to be an effective treatment for CIN2+ across a variety of settings, including in LMICs⁽²⁸⁾.

We have previously learned that women born in far distant continents that move to the USA change their propensity for some chronic diseases like cancer. There is preliminary evidence that the risk for breast cancer among immigrant Asian American women may be higher than among their US-born counterparts. Those who lived more than 50% of their life in the United States were on average 3 times as likely (odds ratio = 3.00; 95% confidence interval, 1.56-5.75) to have breast cancer⁽²⁹⁾.

A randomized trial assessed the outcomes of systematic pelvic and paraaortic lymphadenectomy in patients with advanced ovarian cancer who had undergone intraabdominal macroscopically complete resection and had normal lymph nodes both before and during surgery. The study found no difference in overall nor progression-free survival as compared to no lymphadenectomy. Furthermore, lymphadenectomy was associated with a higher incidence of postoperative complications⁽³⁰⁾.

In a Danish population-based study of 458 646 cancer survivors and 2 121 567 cancer-free controls with up to 17 years of follow-up after cancer diagnosis, cancer survivors of the 12 most common malignancies had a higher risk of hospitalization for a broad range of incident diseases after cancer diagnosis as opposed to their healthy counterparts. This included diseases in the nervous system among breast cancer survivors: hazard ratio, 1.20 and diseases in the respiratory system in lung cancer survivors: HR, 5.85. The difference was most prominent during the first years after the cancer diagnosis⁽³¹⁾.

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