

## EDITORIAL

1. Expert Extraordinary Professor, Facultad de Medicina, Universidad Nacional Mayor de San Marcos, Lima, Perú
2. Honorary Academician, Academia Peruana de Cirugía
3. Editor, Revista Peruana de Ginecología y Obstetricia

ORCID iD: <https://orcid.org/0000-0002-3168-6717>

Financing: Proper of the author

Conflict of interest: None with this paper

Received: 30 December 2018

Accepted: 7 January 2019

Published online: 20 February 2019

Correspondencia:

José Pacheco Romero

✉ [jpachecoperu@yahoo.com](mailto:jpachecoperu@yahoo.com)

Cite: Pacheco-Romero J. From the Editor on recent recommendations on women's health, pregnancy, and the offspring. Rev Peru Ginecol Obstet. 2019; 65(1):5-10 DOI: <https://doi.org/10.31403/rpgo.v65i2143>

# From the Editor on recent recommendations on women's health, pregnancy, and the offspring

## Del Editor sobre recomendaciones recientes para la salud de la mujer, el embarazo y la descendencia

José Pacheco-Romero<sup>1,2,3</sup>, MD, PhD, MSc, FACOG

DOI: <https://doi.org/10.31403/rpgo.v65i2143>

New research in our specialty is complex and exciting, and it is in our interest to share some of it to stimulate research in our countries and institutions. We start the presentation with brief summaries related to women's health.

### ON WOMEN'S HEALTH

#### CHEMICAL PRODUCTS AND REPRODUCTIVE HORMONES

Some chemical products commonly used such as plastics, resins, pesticides, antiseptics, ultraviolet filters and preservatives in cosmetic products may have an impact on reproductive hormone levels in women. Longitudinal urine samples from 143 healthy premenopausal women were measured for bisphenol A (used to make certain plastics and resins, in containers that store food and beverages, such as water bottles), five chlorophenols (used directly or converted into pesticides and as antiseptics; small amounts may be produced when waste water or drinking water is disinfected with chlorine), two ultraviolet (UV) filters, and eight parabens and their metabolites (used as preservatives in cosmetic products) over two menstrual cycles. Four factors -paraben; paraben metabolites and BPA, phenols, and UV filters- were associated with increased progesterone. The paraben factor and the paraben metabolite and BPA factor were associated with increased estradiol. The phenol and UV filter factors were associated with decreased estradiol, FSH, and LH. The UV filter factor showed the strongest inverse association with estradiol. Mixtures of phenols were associated with changes in reproductive hormones<sup>(1)</sup>. Such changes could contribute to adverse health effects in women. Further research is necessary.

#### RESEARCH OF THE CLIMACTERIC IN LATIN AMERICA

For 15 years, the Collaborative Group for Research of the Climacteric in Latin America (REDLINC) has studied several topics including age of menopause, metabolic syndrome, quality of life and climacteric symptoms, sexual dysfunction, poor quality of sleep and insomnia, and use of menopausal hormone therapy (MHT) in the general population, and the knowledge thereof among gynecologists. Data emerged for this region include the age of menopause (49 years), high prevalence of metabolic syndrome (42.9%), and a new waist circumference cut-off value for the Latin American population (88 cm). Sexual dysfunction, poor quality of life and sleep disorders have a prevalence of over 50%, with obesity and sedentary lifestyles as important factors. MHT use is



still low (12.5%). The prevalence of alternative therapy use, recommended by physicians, is high<sup>(2)</sup>.

#### EARLY LIFE EXPOSURE TO FAMINE ON REPRODUCTIVE AGING

We learned from Naeye's studies<sup>(3)</sup> that in cases of maternal severe protein and caloric malnutrition, e.g. the Siege of Leningrad in 1942, and the Dutch Hunger Winter of 1944 to 1945, the newborns weighed less than expected (250 and 500 g less in the examples mentioned). Now, a paper from China associates the effect of early life exposure to famine on reproductive aging in adult women. Between 2011 and 2012, 2 868 women born around the Great Chinese Famine (1956-1964) and exposed to prenatal famine had a higher risk of early menopause (<45 years, OR: 1.59), and a non-significant trend of higher risk of premature ovarian failure (<40 y, OR: 2.07), compared to unexposed women. Such findings provide evidence in favor of the thrifty phenotype hypothesis in reproductive aging and help to better understand the etiology of early menopause<sup>(4)</sup>.

#### VAGINAL REJUVENATION

The FDA warns on a growing number of manufacturers marketing "vaginal rejuvenation" devices to women and claiming these procedures will treat conditions and symptoms related to menopause, urinary incontinence or sexual function. The procedures use laser and other energy-based devices to destroy or reshape vaginal tissue. These products have serious risks, can cause injuries and don't have adequate evidence to support their use for these purposes. The FDA has cleared or approved laser and energy-based devices for the treatment of serious conditions like the destruction of abnormal or pre-cancerous cervical or vaginal tissue, as well as condylomas (genital warts). However, the safety and effectiveness of these devices hasn't been evaluated nor confirmed by the FDA for "vaginal rejuvenation." There are numerous cases of vaginal burns, scarring, pain during sexual intercourse, and recurring or chronic pain. The FDA has recently notified seven device manufacturers (Alma Lasers, BTL Industries, Cynosure, InMode, Sciton, Thermigen and Venus Concept) about inappropriate marketing of their devices for "vaginal

rejuvenation" procedures<sup>(5)</sup>. The American College of Obstetricians and Gynecologists has been warning against "rejuvenation" procedures for years, and recommends physicians inform patients about the lack of data supporting the efficacy and potential complications of vaginal rejuvenation and other similar procedures.

#### SALPINGO-OOPHORECTOMY AND RISK OF COGNITIVE IMPAIRMENT

There could be an increased risk of cognitive impairment or dementia in women who undergo bilateral salpingo-oophorectomy (BSO) before menopause. A nested case-control study of women in the population-based Mayo Clinic Cohort Study of Oophorectomy and Aging-2 (MOA-2) and in the Mayo Clinic Study of Aging (MCSA) in Olmsted County, Minnesota, has evaluated medial temporal lobe structure, white matter lesion load, and  $\beta$ -amyloid deposition in 41 women who underwent BSO before the age of 50 and before reaching natural menopause, and in 49 control participants. Amygdala volume was smaller in the BSO group (median [IQR], 1.74 [1.59-1.91] cm<sup>3</sup>) than in the control group (2.15 [2.05-2.37] cm<sup>3</sup>; P < .001). The parahippocampal-entorhinal cortex was thinner in the BSO group (median [IQR], 3.91 [3.64-4.00] mm) than in the control group (3.97 [3.89-4.28] mm; P = .046). Entorhinal white matter fractional anisotropy was lower in the BSO group (median [IQR], 0.19 [0.18-0.22]) than in the control group (0.22 [0.20-0.23]; P = .03). The authors concluded that abrupt hormonal changes associated with BSO in premenopausal women may lead to medial temporal lobe structural abnormalities later in life. Longitudinal evaluation would help determine whether cognitive decline follows<sup>(6)</sup>.

#### BREASTFEEDING AND WOMEN'S HEALTH

Pregnancy is associated with metabolic changes such as increased insulin resistance, hyperlipidemia, and visceral fat accumulation. Persistence of the metabolic changes that occur during pregnancy has been theorized to increase a woman's lifetime metabolic disease risk. Also, adverse pregnancy outcomes such as preeclampsia, gestational diabetes and preterm delivery are associated with a higher maternal incidence of cardiometabolic diseases later in life. Lactation may play a role in reversing these changes more rapidly. A longer duration



of breastfeeding (exclusively breastfeeding each child for six months and continuing to breastfeed for 12 months) has been associated with a risk reduction in breast cancer, ovarian cancer, endometrial cancer, metabolic syndrome, hypertension, myocardial infarction, and type 2 diabetes. Current suboptimal breastfeeding rates were associated with an excess of 2 619 premature maternal deaths (95% CI 1 978, 3 259)<sup>(7)</sup>. Ob-Gyns should continue promoting exclusive breastfeeding among mothers.

### RECOMMENDATIONS ON SCREENING FOR CERVICAL CANCER

On August 21, 2018, the US Preventive Services Task Force has delivered the following Recommendation Statement on screening for cervical cancer. The USPSTF recommends<sup>(8)</sup>:

- screening for cervical cancer every 3 years with cervical cytology alone in women aged 21 to 29 years
- for women aged 30 to 65 years, screening every 3 years with cervical cytology alone, every 5 years with high-risk human papillomavirus (hrHPV) testing alone, or every 5 years with hrHPV testing in combination with cytology (cotesting) (A recommendation)
- no screening for cervical cancer in women over the age of 65 who have had adequate prior screening and are not otherwise at high risk for cervical cancer (D recommendation)
- no screening for cervical cancer in women younger than 21 years (D recommendation)
- no screening for cervical cancer in women who have had a hysterectomy with removal of the cervix and do not have a history of a high-grade precancerous lesion (ie, cervical intraepithelial neoplasia [CIN] grade 2 or 3) or cervical cancer (D recommendation).

### ON OBSTETRICAL PROBLEMS, PRESENT AND FUTURE

#### INTRAPARTUM CARE FOR A POSITIVE CHILDBIRTH EXPERIENCE

After more than two decades of issuing "Care in normal birth: a practical guide", the

World Health Organization has released a set of 56 recommendations in a report called "Intrapartum Care for a Positive Childbirth Experience". More women are now giving birth in health care facilities and yet suboptimal quality of care continues to impede attainment of the desired health outcomes. In some settings, too few interventions are being provided too late to women, and in other settings women are receiving too many interventions that they do not need, too soon. In line with the targets of Sustainable Development Goal 3 – ensure healthy lives and promote well-being for all at all ages – and the new Global Strategy for Women's, Children's and Adolescents' Health (2016–2030), global agendas are expanding their focus to ensure that women and their babies reach their full potential for health and life. Until now, the concept of "normality" in labor and childbirth is not universal or standardized. That is why one of the recommendations is "to allow a slow labor to continue without trying to hurry the birth along with drugs or other medical interventions." Most women want a physiological labor and birth that can be accomplished without complications, and to have a sense of personal achievement and control through involvement in decision-making, even when medical interventions are needed or wanted<sup>(9)</sup>. Reading these recommendations is heartily encouraged.

#### MEDICAL ERRORS

In line with the symposium on Quality in obstetrical care that we publish in the current number of the RPGO, a paper on the subject states medical errors are estimated to cause 250 000 deaths per year in the US. Previously, research on admitted patients suggested that errors occur due to the way doctors process the data they have about patients - in other words, doctors have the right information, but might not act on it in the best way<sup>(10)</sup>. This refers to the best clinical information and abilities doctors should have in order to obtain and process key symptoms and clinical findings, to appropriately diagnose and treat their patients. The study examined eight months of patient revisits within 72 h of discharge, where patients were admitted and examined on their second visit. Fifty-two cases of confirmed error were identified and classified using a



modified version of the Australian Patient Safety Foundation classification system for medical errors. Faulty information processing was the most frequently identified category of error (45% of cases), followed by faulty verification (31%). Despite the complex nature of diagnostic reasoning, cognitive errors of information processing appear to occur at higher rates than other errors<sup>(11)</sup>.

### PREECLAMPSIA AND TYPE 2 DIABETES MELLITUS

We are aware of the association of preeclampsia and type 2 diabetes mellitus (DM2) in later life<sup>(12)</sup>. One study on the extent to which BMI after pregnancy adds to the elevated risk of post pregnancy DM2 in women with a history of hypertensive disorder of pregnancy (HDP, preeclampsia or gestational hypertension) used data from the Nurses' Health Study II. In women aged 45 to 54 years without prior gestational diabetes mellitus, 6 563 (11.7%) of 56 159 participants had a history of HDP and 1 341 women developed DM2 during 436 333 person-years. BMI was a strong risk factor for DM2 regardless of HDP history. However, there was evidence of an additive interaction between BMI and HDP for the risk of DM2 ( $P = 0.004$ ), with an  $OR=0.12$  in women who were overweight and an  $OR=0.36$  in women with obesity class I<sup>(13)</sup>. We should recommend women with preeclampsia to maintain a healthy weight in order to reduce midlife risk of type 2 diabetes.

### ASPIRIN OR STATIN USE TO MODIFY THE RISK OF STROKE

In order to determine whether aspirin or statin use modified the risk of stroke in the California Teachers Study (CTS), participants under 60 years of age at the time of enrollment in 1995 were followed up prospectively through December 31, 2015. Of 83 749 women under 60 years old at the time of enrollment in 1995, 4 070 (4.9%) had a hypertensive disorder of pregnancy (HDP). Women with prior HDP had an increased risk of stroke (adjusted HR 1.3, 95% CI 1.2, 1.4). There was an interaction ( $p = 0.18$ ) between aspirin use and HDP history on the risk of stroke before age 60: non-users of aspirin had a higher risk (aHR 1.5) while aspirin users did not (aHR 0.8). This effect was not seen with statins<sup>(14)</sup>.

### PARITY AND CARDIOVASCULAR DISEASE RISK

Parity has been reported to play an important role in the development of cardiovascular disease, but results are still controversial. Following a search in the PubMed and Web of Science databases to June 1, 2018, ten cohort studies involving 150 512 incident cases of cardiovascular disease among 3 089 929 participants were included in a meta-analysis. A significant association between parity and cardiovascular disease risk was observed while comparing parity with nulliparity, with a summarised relative risk of 1.14. The summary risk estimates for an increase of one live birth was 1.04, with significant heterogeneity. Findings suggest that ever parity is related to cardiovascular disease risk, and there is an association between the number of pregnancies and the cardiovascular disease risk<sup>(15)</sup>.

### MOTHERS OF INFANTS BORN WITH A MAJOR CONGENITAL ANOMALY

In a cohort study of 471 344 Danish women, 42 943 mothers of infants born with a major congenital anomaly, after a median follow-up of 19.5 years, had a 15% increased risk of acute myocardial infarction, coronary revascularization, or stroke, compared with 428 401 women without an affected infant. This elevated risk rose to 37% among women who gave birth to more severely affected infants with multiorgan congenital anomalies<sup>(16)</sup>. This life-changing and stressful event has to be considered in the clinical follow-up of the mother.

### THE OFFSPRING

#### BIRTH BY CESAREAN DELIVERY AND RISK OF CHILDHOOD OBESITY

Nearly 1 in 5 children worldwide<sup>(17)</sup> and 1 in 3 children in the United States<sup>(18)</sup> are born by cesarean delivery. Birth by cesarean delivery is associated with a higher risk of childhood obesity. Two meta-analyses<sup>(19,20)</sup> summarizing data from 24 studies have reported an increased risk of obesity for individuals born by cesarean section ( $OR: 1.33$ ; 95%CI, 1.19-1.48 and 1.22; 95%CI, 1.05-1.42), with little difference for risk of obesity during childhood versus adolescence, and some evidence that the elevated risk persists in adult life (odds ratio, 1.50; 95%CI, 1.02-2.20)<sup>(21)</sup>.



## BREAST MILK EXPOSURE IN PRETERM NEONATES AND BRAIN STRUCTURE AND CONNECTIVITY

Preterm infants are at an increased risk of alterations in brain structure and connectivity, and subsequent neurocognitive impairment. Breast milk may be more advantageous than formula for promoting brain development in infants born at term. In a study of neonatal breast milk exposure, a brain MRI was taken at term-equivalent age in 47 preterm infants (mean postmenstrual age [PMA] 29.43 weeks, range 23.28–33.0). Twenty-seven infants received exclusive breast milk feeds for at least 75% of their in-patient care stance. This was associated with higher connectivity in the fractional anisotropy (FA)-weighted connectome compared with the group who had less than 75% of days receiving exclusive breast milk feeds (NBS,  $p = 0.04$ ). Within the TBSS white matter skeleton, the group that exclusively received breast milk over 75% of days exhibited higher FA within the corpus callosum, cingulum cingulate gyri, centrum semiovale, corticospinal tracts, arcuate fasciculi and posterior limbs of the internal capsule compared with the low exposure group after adjustment for PMA at birth, PMA at image acquisition, bronchopulmonary dysplasia, and chorioamnionitis ( $p < 0.05$ ). This study concluded that breast milk feeding in the weeks after preterm birth is associated with improved structural connectivity of developing networks and greater FA in major white matter fasciculi<sup>(22)</sup>.

## PATERNAL DEPRESSION IN THE POSTNATAL PERIOD AND OFFSPRING DEPRESSION

In a prospective cohort study of 3 176 British father-offspring pairs (the Avon Longitudinal Study of Parents and Children), paternal depression in the postnatal period (at 8 weeks after the birth of their children) was associated with offspring depression at the age of 18 and appears to exert its influence on later emotional problems in female children, partially through maternal depression. The association is mediated by maternal depression at 8 months after birth and conduct problems at 42 months after birth<sup>(23)</sup>. Early conduct disorder in children appears to be a mechanism of risk transmission, and should be taken into account by pediatricians, gynecologists and physicians. Also, it is recommended to consider the partner when a parent presents with depression.

## REFERENCES

1. Pollack AZ, Mumford SL, Krall JR, Carmichael AE, Sjaarda LA, Perkins NJ, Kannan K, Schisterman EF. Exposure to bisphenol A, chlorophenols, benzophenones, and parabens in relation to reproductive hormones in healthy women: A chemical mixture approach. *Envir Intern*. 2018 Nov;120:137-44. <https://doi.org/10.1016/j.envint.2018.07.028>Get rights and content
2. Tserotas K, Blümel JE. Menopause research in Latin America. *Climacteric*. 2018 Dec 21:1-5. doi: 10.1080/13697137.2018.1540565
3. Naeye RL. Maternal nutrition and pregnancy outcome. In: J. Dobbing, editor. *Maternal Nutrition in Pregnancy: Eating for Two?* Academic Press, London. 1981:89–111.
4. Wang N, Huang Y, Wen J, Su Q, Huang Y, Cai L, et al. Early life exposure to famine and reproductive aging among Chinese women. *Menopause: December 3, 2018 - Volume Publish Ahead of Print - Issue - p*. doi: 10.1097/GME.0000000000001259
5. U. S. Federal Drug Administration Statement. Statement from FDA Commissioner Scott Gottlieb, M.D., on efforts to safeguard women's health from deceptive health claims and significant risks related to devices marketed for use in medical procedures for "vaginal rejuvenation". Statement was updated on Aug. 2, 2018 to reflect a correction in the listing of manufacturers that received a letter from the FDA. <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm615130.htm>
6. Zeydan B, Tosakulwong N, Schwarz CG, Senjem, ML, Gunter JL, Reid RI, et al. Association of bilateral salpingo-oophorectomy before menopause onset with medial temporal lobe neurodegeneration. *JAMA Neurol*. October 2018. DOI: 10.1001/jamaneurol.2018.3057
7. Louis-Jacques A, Stuebe A. Long-term maternal benefits of breastfeeding. *Contemporary Ob/Gyn*. Jul 11, 2018;64(7). [http://www.contemporaryobgyn.net/breast-health/long-term-maternal-benefits-breastfeeding?rememberme=1&elq\\_mid=5014&elq\\_cid=576909US](http://www.contemporaryobgyn.net/breast-health/long-term-maternal-benefits-breastfeeding?rememberme=1&elq_mid=5014&elq_cid=576909US)
8. Preventive Services Task Force. Screening for Cervical Cancer. US Preventive Services Task Force Recommendation Statement. *JAMA*. 2018;320(7):674-686. doi:10.1001/jama.2018.10897
9. World Health Organization. WHO recommendations: intrapartum care for a positive childbirth experience. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO. <http://apps.who.int/iris/bitstream/handle/10665/260178/9789241550215-eng.pdf?sequence=1>
10. De Gruyter. Medical errors in the emergency room: Understanding why 250,000 deaths per year are caused by medical error -- what causes these errors in emergency departments? *EurekAlert*. Public release: 27-jul-2018. <https://doi.org/10.1515/dx-2018-0011>
11. Schnapp BH, Sun JE, Kim JL, Strayer RJ, Shah KH. Cognitive error in an academic emergency department. *De Gruyter Diagnosis*: 2018;5(3):135-42. Published Online: 2018-07-17 | DOI: <https://doi.org/10.1515/dx-2018-0011>
12. Wang Z, Wang Z, Wang L, Qiu M, Wang Y, Hou X, Guo Z,



- Wang B. Hypertensive disorders during pregnancy and risk of type 2 diabetes in later life: a systematic review and meta-analysis. *Endocrine*. 2017 Mar;55(3):809-821. doi: 10.1007/s12020-016-1075-6
13. Timpka S, Stuart JJ, Tanz LJ, Hu FB, Franks FW, Rich-Edwards JW. Postpregnancy BMI in the progression from hypertensive disorders of pregnancy to type 2 diabetes. *Diabetes Care*. 2018 Nov; dc181532. <https://doi.org/10.2337/dc18-1532>
  14. Miller EC, Boehme AK, Chung NT, Wang SS, Lacey JV, Lakshminarayan K, Zhong C, Woo D, Bello NA, Wapner R, Elkind MSV, Willey JZ. Aspirin reduces long-term stroke risk in women with prior hypertensive disorders of pregnancy. *Neurology* Dec 2018, 10.1212/WNL.0000000000006815; DOI: 10.1212/WNL.0000000000006815
  15. Li W, Ruan W, Lu Z, Wang D. Parity and risk of maternal cardiovascular disease: A dose-response meta-analysis of cohort studies. *Eur J Prev Cardiol*. First Published December 19, 2018. <https://doi.org/10.1177/2047487318818265>.
  16. Cohen E, Horváth-Puhó E, Ray JG, Pedersen L, Ehrenstein V, Adler N, Vigod S, et al. Cardiovascular disease among women who gave birth to an infant with a major congenital anomaly. *JAMA Netw Open*. 2018;1(5):e182320. doi:10.1001/jamanetworkopen.2018.2320
  17. Betrán AP, Ye J, Moller AB, Zhang J, Gülmezoglu AM, Torloni MR. The increasing trend in caesarean section rates: global, regional and national estimates: 1990-2014. *PLoS One*. 2016;11(2):e0148343. doi:10.1371/journal.pone.0148343
  18. Martin JA, Hamilton BE, Osterman MJK, Driscoll AK, Drake P. Births: final data for 2016. *Natl Vital Stat Rep*. 2018;67(1):1-55.
  19. Darmasseelane K, Hyde MJ, Santhakumaran S, Gale C, Modi N. Mode of delivery and offspring body mass index, overweight and obesity in adult life: a systematic review and meta-analysis. *PLoS One*. 2014;9(2):e87896. doi:10.1371/journal.pone.0087896
  20. Li HT, Zhou YB, Liu JM. The impact of cesarean section on offspring overweight and obesity: a systematic review and meta-analysis. *Int J Obes (Lond)*. 2013;37(7):893-899. doi:10.1038/ijo.2012.195
  21. Mitchell C, Chavarro JE. mode of delivery and childhood obesity. is there a cause for concern? *JAMA Network Open*. *Pediatrics*. Published: November 21, 2018. doi:10.1001/jamanetworkopen.2018.5008
  22. Blesa M, Sullivan G, Anblagan D, Emma J, Telford EJ, Quigley AJ, Sparrow SA, et al. Early breast milk exposure modifies brain connectivity in preterm infants. *NeuroImage*. 2019 Jan; 184:431-9. <https://doi.org/10.1016/j.neuroimage.2018.09.045>
  23. Gutierrez-Galve L, Stein A, Hanington L, Heron J, Lewis G, O'Farrelly C, Ramchandani PG. Association of maternal and paternal depression in the postnatal period with offspring depression at age 18 years. *JAMA Psychiatry*. Published online December 26, 2018. doi:10.1001/jamapsychiatry.2018.3667