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Auxiliary and Experimental Diagnostic Techniques for Hydatidiform Moles

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Hydatidiform moles are classified into complete hydatidiform moles (CHMs), which are androgenetic and diploid, and partial hydatidiform moles (PHM), which are triploid with two paternal chromosomes and one maternal chromosome. The incidence of gestational trophoblastic neoplasia differs substantially between CHM and PHM. However, they are occasionally difficult to diagnose. In this review, auxiliary and experimental methods based on cytogenetic features and advanced molecular detection techniques applied to the diagnosis and analysis of hydatidiform moles are summarized, including basic principles, characteristics, and clinical implications. Short tandem repeat polymorphism analysis is considered the gold standard for the genetic diagnosis of hydatidiform moles. In clinical settings, immunohistochemical analyses of p57^{KIP2}, an imprinted gene product, are widely used to differentiate CHMs from other conceptuses, including PHMs. Recently, new molecular genetic techniques, such as single nucleotide polymorphism arrays, have been applied to research on hydatidiform moles. In addition to insights from classical methods, such as chromosome analysis, recently developed approaches have yielded novel findings related to the mechanism underlying the development of androgenetic CHMs.

Maternal Vaccination - Current Status, Challenges, And Opportunities

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Aim: Maternal vaccination is a promising strategy for protecting pregnant women and newborns against severe infections. This review aims to describe the

current status and challenges associated with maternal vaccination against seasonal influenza, tetanus-diphtheria-pertussis (Tdap/DTaP), and novel coronavirus disease of 2019 (COVID-19) in Japan and other countries, mainly the United States and the United Kingdom.

Methods: A literature search was conducted in PubMed and other public websites (e.g., Centers for Disease Control and Prevention) to obtain information on maternal vaccination.

Results: Inactivated vaccines are recommended for pregnant women by gynecologic societies in Japan, the United States, and the United Kingdom. Among pregnant Japanese women, the influenza and COVID-19 (two doses) vaccine coverage rates were 27.0%–53.5% (six studies) and 73.6% (one study), respectively; there are no studies on maternal vaccination with DTaP. Concerns regarding vaccine safety are a major barrier to maternal vaccination across countries. Maternal vaccination is effective in preventing severe disease in pregnant women and protecting infants aged <6 months, is generally safe, and does not increase the risk of adverse maternal and fetal outcomes. Providing accurate information regarding vaccination through healthcare providers and the government and government funding for vaccines may help improve maternal vaccination rates in Japan.

Conclusion:

Current coverage for maternal vaccination is still low globally mainly because of vaccine hesitancy among pregnant women. The government, drug-regulatory authorities, and healthcare professionals must educate pregnant women about the effectiveness and safety of maternal vaccines and encourage vaccination when the benefits outweigh the risks.

Mifepristone and Misoprostol for Undesired Pregnancy of Unknown Location

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Objective: To compare immediate initiation with delayed initiation of medication abortion among

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patients with an undesired pregnancy of unknown location.

Methods: This retrospective cohort study used electronic medical record data from the Planned Parenthood League of Massachusetts (2014–2019) for patients who requested medication abortion with a last menstrual period (LMP) of 42 days or less and pregnancy of unknown location (no gestational sac) on initial ultrasonogram. Clinicians could initiate medication abortion with mifepristone followed by misoprostol while simultaneously excluding ectopic pregnancy with serial serum human chorionic gonadotropin (hCG) testing (same-day-start group) or establish a diagnosis with serial hCG tests and repeat ultrasonogram before initiating treatment (delay-for-diagnosis group). We compared primary safety outcomes (time to diagnosis of pregnancy location [rule out ectopic], emergency department visits, adverse events, and nonadherence with follow-up) between groups. We also reported secondary efficacy outcomes: time to complete abortion, successful medication abortion (no uterine aspiration), and ongoing pregnancy.

Results: Of 5,619 medication abortion visits for patients with an LMP of 42 days or less, 452 patients had pregnancy of unknown location (8.0%). Three patients underwent immediate uterine aspiration, 55 had same-day start, and 394 had delay for diagnosis. Thirty-one patients (7.9%), all in the delay-for-diagnosis group, were treated for ectopic pregnancy, including four that were ruptured. Among patients with no major ectopic pregnancy risk factors (n=432), same-day start had shorter time to diagnosis (median 5.0 days vs 9.0 days; $P=.005$), with no significant difference in emergency department visits (adjusted odds ratio [aOR] 0.90, 95% CI 0.43–1.88) or nonadherence with follow-up (aOR 0.92, 95% CI 0.39–2.15). Among patients who proceeded with abortion (n=270), same-day start had shorter time to complete abortion (median 5.0 days vs 19.0 days; $P<.001$). Of those who had medication abortion with known outcome (n=170), the rate of successful medication abortion was lower (85.4% vs 96.7%; $P=.013$) and the rate of ongoing pregnancy was higher (10.4% vs 2.5%; $P=.041$) among patients in the same-day-start group.

Conclusion: In patients with undesired pregnancy of unknown location, immediate initiation of medication abortion is associated with more rapid exclusion of

ectopic pregnancy and pregnancy termination but lower abortion efficacy.

Alternatives to Hysterectomy in Patients With Uterovaginal Prolapse

Baburam Dixit Thapa, Tulasa Basnet, G. Willy Davila, Mohan Chandra Regmi .J Clin Gynecol Obstet. 2022;11(3):53-61 doi: <https://doi.org/10.14740/jcg0795>

Background: Uterovaginal prolapse is a common problem in women. Hysterectomy has been considered as a standard procedure during surgical management of pelvic organ prolapse. However, in recent years, interest has been growing in the use of uterus-preserving surgeries. Different options available for uterine preservation include the Manchester Fothergill's operation, sacral hysteropexy (abdominal, laparoscopic or robotic with or without mesh), uterosacral ligament hysteropexy, sacrospinous hysteropexy (with or without mesh) and colpocleisis. The aim of this review was to analyze the different options of uterus-preserving surgeries and compare their outcomes with prolapse surgeries including hysterectomy.

Methods: PubMed, MEDLINE, Clinical trials.gov and the Hinari database were reviewed through 2020 by two of the authors. Only randomized controlled trials (RCTs) or non-randomized prospective controlled studies (nrPCSSs) where different uterus-preserving surgeries for uterovaginal prolapse were compared with surgeries involving hysterectomy were included for the review.

Results: We identified 225 articles from the electronic search and 19 articles meeting the inclusion and exclusion criteria were reviewed. Among them, 10 were RCTs and nine were nrPCSSs. The review identified that objective prolapse recurrence, quality of life and adverse events were similar between uterine preservation and hysterectomy groups. Abdominal routes were non-inferior to vaginal uterus-preserving surgeries. Need for repeat surgery after a hysteropexy procedure ranged from 2% to 29%. The Manchester operation demonstrated good anatomical and symptomatic improvement as compared to hysterectomy. When comparing sacrohysteropexy routes, the laparoscopic approach had lower recurrent prolapse symptoms than open sacrohysteropexy. Operating time and estimated blood loss were less with uterus-preserving surgeries. The most common

adverse events in hysteropexy surgeries were urinary incontinence, voiding dysfunction, sexual dysfunction and mesh erosion, when mesh us.

Conclusion: The evidence from currently available literature suggests the vaginal and abdominal uterus-preserving surgeries to be equally effective, and not inferior to surgical procedures including hysterectomy. When surgeons are faced with a patient requesting uterine preservation, counseling should be performed cautiously regarding choosing one type of hysteropexy over another. However, the data on long-term follow-up and outcomes are lacking.

Keywords: Hysterectomy; Sacrohysteropexy; Uterus-preserving surgeries; Uterine su

Relugolix Combination Therapy for Uterine Leiomyoma–Associated Pain in the LIBERTY Randomized Trials

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Objective: To assess the effect of once-daily relugolix combination therapy (relugolix-CT: relugolix 40 mg, estradiol 1 mg, and norethindrone acetate 0.5 mg) compared with placebo on moderate-to-severe pain in women with uterine leiomyomas and heavy menstrual bleeding.

Methods: Two replicate, multinational, double-blind, 24-week, randomized, phase 3 studies (LIBERTY 1 and 2) were conducted in premenopausal women with uterine leiomyoma–associated heavy menstrual bleeding (80 mL or greater per cycle for two cycles or 160 mL or greater during one cycle). A predefined secondary objective was to determine the effect of relugolix-CT on moderate-to-severe uterine leiomyoma–associated pain in the pain subpopulation (women with maximum pain scores of 4 or higher on the 0–10 numerical rating scale at baseline, with pain score reporting compliance of 80% (ie, 28 days or more over the last 35 days of treatment). This key secondary endpoint was defined as the proportion of women achieving minimal-to-no uterine leiomyoma–associated pain (maximum numerical rating scale score 1 or lower) at week 24; menstrual and

nonmenstrual pain were evaluated in prespecified secondary analyses. Treatment comparisons were performed in the pooled LIBERTY 1 and 2 pain subpopulation using the Cochran-Mantel-Haenszel test stratified by baseline menstrual blood loss volume.

Results: Across both trials, 509 women were randomized to relugolix-CT or placebo (April 2017–December 2018). Of these, 277 (54.4%) met pain subpopulation requirements. With relugolix-CT, 45.2% (95% CI 36.4–54.3) of women achieved minimal-to-no pain compared with 13.9% (95% CI 8.8–20.5) with placebo (nominal $P<.001$). The proportions of women with minimal-to-no pain during menstrual days and during nonmenstrual days were significantly higher with relugolix-CT (65.0% [95% CI 55.6–73.5] and 44.6% [95% CI 32.3–57.5], respectively) compared with placebo (19.3% [95% CI 13.2–26.7], nominal $P<.001$, and 21.6% [95% CI 12.9–32.7], nominal $P=.004$, respectively).

Conclusion: Over 24 weeks, relugolix-CT significantly reduced moderate-to-severe uterine leiomyoma–associated pain with a more pronounced effect on menstrual pain. These data support that relugolix-CT had clinically meaningful effects on women's experience of uterine leiomyoma–associated pain.

The importance of nutrition in pregnancy and lactation: lifelong consequences

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Most women in the United States do not meet the recommendations for healthful nutrition and weight before and during pregnancy. Women and providers often ask what a healthy diet for a pregnant woman should look like. The message should be “eat better, not more.” This can be achieved by basing diet on a variety of nutrient-dense, whole foods, including fruits, vegetables, legumes, whole grains, healthy fats with omega-3 fatty acids that include nuts and seeds,

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and fish, in place of poorer quality highly processed foods. Such a diet embodies nutritional density and is less likely to be accompanied by excessive energy intake than the standard American diet consisting of increased intakes of processed foods, fatty red meat, and sweetened foods and beverages. Women who report "prudent" or "health-conscious" eating patterns before and/or during pregnancy may have fewer pregnancy complications and adverse child health outcomes. Comprehensive nutritional supplementation (multiple micronutrients plus balanced protein energy) among women with inadequate nutrition has been associated with improved birth outcomes, including decreased rates of low birthweight. A diet that severely restricts any macronutrient class should be avoided, specifically the ketogenic diet that lacks carbohydrates, the Paleo diet because of dairy restriction, and any diet characterized by excess saturated fats. User-friendly tools to facilitate a quick evaluation of dietary patterns with clear guidance on how to address dietary inadequacies and embedded support from trained healthcare providers are urgently needed.

Recent evidence has shown that although excessive gestational weight gain predicts adverse perinatal outcomes among women with normal weight, the degree of prepregnancy obesity predicts adverse perinatal outcomes to a greater degree than gestational weight gain among women with obesity. Furthermore, low body mass index and insufficient gestational weight gain are associated with poor perinatal outcomes. Observational data have shown that first-trimester gain is the strongest predictor of adverse outcomes. Interventions beginning in early pregnancy or preconception are needed to prevent downstream complications for mothers and their children. For neonates, human milk provides personalized nutrition and is associated with short- and long-term health benefits for infants and mothers. Eating a healthy diet is a way for lactating mothers to support optimal health for themselves and their infants.

Key words: adolescent pregnancy, developmental origins of disease, fetal and neonatal nutrition, gestational diabetes mellitus lactation, macronutrients, maternal nutrition, micronutrients, nutritional requirements pregnancy, vitamin supplementation.

Michal Fishel Bartal, Bahia M. Sibai, Eclampsia in the 21st century,

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The reported incidence of eclampsia is 1.6 to 10 per 10,000 deliveries in developed countries, whereas it is 50 to 151 per 10,000 deliveries in developing countries. In addition, low-resource countries have substantially higher rates of maternal and perinatal mortalities and morbidities. This disparity in incidence and pregnancy outcomes may be related to universal access to prenatal care, early detection of preeclampsia, timely delivery, and availability of healthcare resources in developed countries compared to developing countries. Because of its infrequency in developed countries, many obstetrical providers and maternity units have minimal to no experience in the acute management of eclampsia and its complications. Therefore, clear protocols for prevention of eclampsia in those with severe preeclampsia and acute treatment of eclamptic seizures at all levels of healthcare are required for better maternal and neonatal outcomes. Eclamptic seizure will occur in 2% of women with preeclampsia with severe features who are not receiving magnesium sulfate and in <0.6% in those receiving magnesium sulfate. The pathogenesis of an eclamptic seizure is not well understood; however, the blood-brain barrier disruption with the passage of fluid, ions, and plasma protein into the brain parenchyma remains the leading theory. New data suggest that blood-brain barrier permeability may increase by circulating factors found in preeclamptic women plasma, such as vascular endothelial growth factor and placental growth factor. The management of an eclamptic seizure will include supportive care to prevent serious maternal injury, magnesium sulfate for prevention of recurrent seizures, and promoting delivery. Although routine imaging following an eclamptic seizure is not recommended, the classic finding is referred to as the posterior reversible encephalopathy syndrome. Most patients with posterior reversible encephalopathy syndrome will show complete resolution of the imaging finding within 1 to 2 weeks, but routine imaging follow-up is unnecessary unless there are findings of intracranial hemorrhage, infarction, or ongoing neurologic deficit. Eclampsia is associated with increased risk of maternal mortality and morbidity, such

as placental abruption, disseminated intravascular coagulation, pulmonary edema, aspiration pneumonia, cardiopulmonary arrest, and acute renal failure. Furthermore, a history of eclamptic seizures may be related to long-term cardiovascular risk and cognitive difficulties related to memory and concentration years after the index pregnancy. Finally, limited data suggest that placental growth factor levels in women with preeclampsia are superior to clinical markers in prediction of adverse pregnancy outcomes. This data may be extrapolated to the prediction of eclampsia in future studies.

This summary of available evidence provides data and expert opinion on possible pathogenesis of eclampsia,

imaging findings, differential diagnosis, and stepwise approach regarding the management of eclampsia before delivery and after delivery as well as current recommendations for the prevention of eclamptic seizures in women with preeclampsia.

Key words: Abruptio, angiogenic, cardiovascular, cerebral edema, convulsions, fetal death, fetal growth restriction, hypertensive disorder of pregnancy, magnesium sulfate, maternal mortality, placental growth factor, posterior reversible encephalopathy syndrome, seizures, severe maternal morbidity, soluble endoglin, soluble fms-like tyrosine kinase-1, vascular endothelial growth factor