Introduction to the Guest Editors of the American Journal of Obstetrics & Gynecology Supplement on Preeclampsia 2022
Roberto Romero

Preeclampsia and eclampsia: the conceptual evolution of a syndrome
Offer Erez; Roberto Romero; Eunjung Jung; Piya Chaemsaithong; Mariachiara Bosco; Manaphat Suksai; Dahiana M. Gallo; Francesca Gotsch
This study describes the conceptual evolution of preeclampsia and eclampsia and reviews the scientific basis for the diagnostic criteria and implications of vascular dysfunction during pregnancy.

The assessment of blood pressure in pregnant women: pitfalls and novel approaches
Alice Hurrell; Louise Webster; Lucy C. Chappell; Andrew H. Shennan
This review article gives a detailed description of the technique of assessing blood pressure in pregnant women. Potential sources of inaccurate measurement are outlined and novel developments and technologies are discussed.

Proteinuria during pregnancy: definition, pathophysiology, methodology, and clinical significance
Michal Fishel Bartal; Marshall D. Lindheimer; Baha M. Sibai
After reviewing the available data, the most important factor that influences maternal and neonatal outcome is the severity of blood pressures and presence of end organ damage, rather than the excess protein excretion. Since, the management of gestational hypertension and preeclampsia without severe features is almost identical in frequency of surveillance and timing of delivery, the separation into 2 disorders is unnecessary.

The evolution of the diagnostic criteria of preeclampsia-eclampsia
Michael S. Tanner; Mary-Ann Davey; Ben W. Mol; Daniel L. Rolnik
The diagnostic criteria for preeclampsia have evolved substantially over time but have often been guided by expert opinion and consensus rather than by primary data.

Original research articles, whose abstracts appear in this issue, are posted in full at ajog.org
The etiology of preeclampsia
Eunjung Jung; Roberto Romero; Lami Yeo; Nardhy Gomez-Lopez; Piya Chaemsaithong; Adithep Jaovisidha; Francesca Gotsch; Offer Erez
This article describes the causal risk factors, or etiology, of preeclampsia.

Progress in the understanding of the pathophysiology of immunologic maladaptation related to early-onset preeclampsia and metabolic syndrome related to late-onset preeclampsia
Pierre-Yves Robillard; Gustaaf Dekker; Marco Scioscia; Shigeru Saito
Update on the progresses in immunology of reproduction (partial trophoblastic implantation failure in early-onset preeclampsia) and metabolic syndrome for late onset preeclampsia.

Does race or ethnicity play a role in the origin, pathophysiology, and outcomes of preeclampsia? An expert review of the literature
Jasmine D. Johnson; Judette M. Louis
Black race, a social construct, has been associated with a higher prevalence of preeclampsia and perinatal morbidity, however, few studies have addressed the underlying drivers for this association or interventions for improvement.

Decidualization resistance in the origin of preeclampsia
Tamara Garrido-Gómez; Nerea Castillo-Maro; Teresa Cordero; Carlos Simón
The maternal decidua contributes to the pathogenesis of pregnancy disorders, including severe preeclampsia.

Failure of physiological transformation and spiral artery atherosis: their roles in preeclampsia
Anne Cathrine Staff; Heidi E. Fjeldstad; Ingrid Knutsdotter Fosheim; Kjartan Moe; Gitta Turowski; Guro Mørk Johnsen; Patji Alnaes-Katjavivi; Meryam Sugulle
Preeclampsia spiral artery remodeling defects and acute atherosis are summarized. Remaining enigmas, including implications for long-term maternal health are discussed.

Syncytiotrophoblast stress in preeclampsia: the convergence point for multiple pathways
Christopher W. G. Redman; Anne Cathrine Staff; James M. Roberts
Syncytiotrophoblast stress is the key pathology of preeclampsia and related syndromes. Most presentations result from mal-placentation (early onset preeclampsia) or placental aging, which is a universal process that contributes to what we call the 'Twilight Placenta' and underlies (late onset preeclampsia).

Placental energy metabolism in health and disease—significance of development and implications for preeclampsia
Irving L. M. H. Aye; Catherine E. Aiken; D. Stephen Charnock-Jones; Gordon C. S. Smith
Understanding placental energy metabolism may explain many of the phenotypes that are associated with preeclampsia and provide new insights into future therapeutic strategies.

Activation of the pregnancy-specific expression of protease-activated receptor 1 can explain clinical symptoms of preeclampsia and should be considered as a therapeutic target.

S954 The placenta and preeclampsia: villain or victim? Karen Melchiorre; Veronica Giorgione; Basky Thilaganathan

Maternal cardiovascular maladaptation resulting in uteroplacental hypoperfusion is the etiological step which leads to placental dysfunction and preeclampsia. Therefore, the placenta is the victim and not the villain in the development of preeclampsia.

S963 An integrated model of preeclampsia: a multifaceted syndrome of the maternal cardiovascular-placental-fetal array Simcha Yagel; Sarah M. Cohen; Debra Goldman-Wohl

We reviewed the maternal-placental-fetal array that showed how any disruption in any component or nexus may lead to the syndrome of preeclampsia.

S973 Animal models of preeclampsia: investigating pathophysiology and therapeutic targets Bhavisha A. Bakrania; Eric M. George; Joey P. Granger

Animal models remain a critical tool in understanding the pathophysiology of preeclampsia, and identifying therapeutic targets for its treatment. This review discusses models of placental ischemia, angiogenic imbalance, immune activation, and others in rodents and nonhuman primates, all of which have made valuable contributions to our understanding of clinical manifestation of preeclampsia.

S988 Hemodynamic pathways of gestational hypertension and preeclampsia Wilfried Gyselaers

Reported evidence is summarized on intravascular volume or vascular tone as primary causes of gestational hypertension and preeclampsia.

S1006 Preeclampsia has two phenotypes which require different treatment strategies Giulia Masini; Lin F. Foo; Jasmine Tay; Ian B. Wilkinson; Herbert Valensise; Wilfried Gyselaers; Christoph C. Lees

Preeclampsia exists as 2 phenotypes that have diametrically contrasting hemodynamic observations with respect to the cardiac output, vascular resistance, arterial function, and intravascular volume.

S1019 Imbalances in circulating angiogenic factors in the pathophysiology of preeclampsia and related disorders Sarosh Rana; Suzanne D. Burke; S. Ananth Karumanchi

Excess antiangiogenic factors of placental origin contributes to hypertension, proteinuria, and preeclampsia-related adverse outcomes. Measurement of antiangiogenic and proangiogenic factors in maternal circulation may help clinicians in the early diagnosis and prognosis of preeclampsia and related disorders.

(continued)
Discovery of antiangiogenic factors in the pathogenesis of preeclampsia
S. Ananth Karumanchi; Towia Libermann

Real-world data on the clinical use of angiogenic factors in pregnancies with placental dysfunction
Anne Dathan-Stumpf; Victoria Czarnowsky; Vicky Hein; Theresa Andraczek; Holger Stepan
In a real-world setting, the soluble fms-like tyrosine kinase-1 to placental growth factor ratio could be used as a supplemental tool to help estimate the severity of placental dysfunction.

The diagnostic value of angiogenic and antiangiogenic factors in differential diagnosis of preeclampsia
Stefan Verlohren; Lisa-Antonia Droge
The soluble fms-like tyrosine kinase-1 to placental growth factor ratio is a clinical value tool to predict and diagnose preeclampsia and preeclampsia-associated adverse outcomes.

Complement activation and regulation in preeclampsia and hemolysis, elevated liver enzymes, and low platelet count syndrome
Richard M. Burwick; Bruce B. Feinberg
Existing data link preeclampsia and hemolysis, elevated liver enzymes, and low platelet count syndrome with increased activation of the terminal complement pathway which, in some cases, may be influenced by genetic alterations in complement regulators. Targeted inhibition of the complement pathway may be an effective strategy to treat disease, but this approach warrants evaluation in clinical trials.

First trimester preeclampsia screening and prediction
Piya Chaemsaithong; Daljit Singh Sahota; Liona C. Poon
The best method for the identification of high-risk women for preterm preeclampsia is one that utilizes the Bayes theorem-based method that combines maternal factors and biomarkers. This approach has been extensively externally validated.

Ophthalmic artery Doppler in the prediction of preeclampsia
Kypros H. Nicolaides; Manoel Sarno; Alan Wright
Ophthalmic artery Doppler provides a useful biomarker for the prediction of preeclampsia.

The prediction of preeclampsia: the way forward
Leslie Myatt
A strategy is presented for collecting standardized clinical data and biospecimens from very large patient numbers in both high and low resource settings, employing novel data collection and analytical tools, to hence define the heterogeneous subtypes encompassed by the preeclampsia syndrome leading to phenotype-specific prediction and treatment.

Prevention of preeclampsia with aspirin
Daniel L. Rolnik; Kypros H. Nicolaides; Liona C. Poon
Aspirin prevents preterm preeclampsia when administered before 16 weeks of gestational age to high-risk women at doses >100 mg.
When to give aspirin to prevent preeclampsia: application of Bayesian decision theory
David Wright; Alan Wright; Min Yi Tan; Kypros H. Nicolaides
Screening for preterm preeclampsia and treatment of the high-risk group was preferable to no treatment and universal treatment.

Low-molecular-weight heparin for prevention of preeclampsia and other placenta-mediated complications: a systematic review and meta-analysis
Monica Cruz-Lemini; Juan Carlos Vázquez; Johana Ullmo; Elisa Llurba
Low-molecular-weight heparin decreases the risk of preeclampsia and other placenta-mediated complications in high-risk women.

Circulating maternal placental growth factor responses to low-molecular-weight heparin in pregnant patients at risk of placental dysfunction
Kelsey McLaughlin; Sebastian R. Hobson; Anjana Ravi Chandran; Swati Agrawal; Rory C. Windrim; W. Tony Parks; Adrian W. Bowman; Ulla Sovio; Gordon C. Smith; John C. Kingdom
Prophylactic low-molecular-weight heparin may augment deficient circulating placental growth factor in second-trimester high-risk pregnancies and may prolong pregnancy compared with untreated patients.

Pravastatin, proton-pump inhibitors, metformin, micronutrients, and biologics: new horizons for the prevention or treatment of preeclampsia
Stephen Tong; Tu’uhevaha J. Kaitu’u-Lino; Roxanne Hastie; Fiona Brownfoot; Catherine Cluver; Natalie Hannan
There has been increasing research to identify new therapeutic agents for the prevention or treatment of preeclampsia, ranging from preclinical studies to phase III trials and mainly focusing on drug repurposing.

The role of statins in the prevention of preeclampsia
Devin D. Smith; Maged M. Costantine
In this article we review the mechanisms of action, preclinical and clinical evidence, and safety profile for statin use in the prevention of preeclampsia.

Chronic hypertension and superimposed preeclampsia: screening and diagnosis
Nikos A. Kametas; Diane Nzelu; Kypros H. Nicolaides
Renal, cardiac, angiogenic, and inflammatory biomarkers in women with chronic hypertension have not been proven useful so far in the screening and diagnosis of superimposed preeclampsia.

Toward personalized management of chronic hypertension in pregnancy
Laura A. Magee; Asma Khalil; Nikos Kametas; Peter von Dadelszen
Personal characteristics, symptoms, blood pressure (BP) features beyond the BP level, and other physiological characteristics are associated with adverse outcomes and offer opportunities to personalize care.
Postpartum preeclampsia or eclampsia: defining its place and management among the hypertensive disorders of pregnancy
Alisse Hauspurg; Arun Jeyabalan
We review the etiology, risk factors, clinical manifestations, management, and outcomes for pregnancies complicated by new-onset postpartum preeclampsia or eclampsia.

Guidelines—similarities and dissimilarities: a systematic review of international clinical practice guidelines for pregnancy hypertension
Georgia Scott; Tessa E. Gillon; Anouk Pels; Peter von Dadelszen; Laura A. Magee
Pregnancy hypertension guidelines are increasingly aligned, although key differences remain, related to whether and how preeclampsia severity is defined, biomarkers are incorporated into time-of-disease assessment, and blood pressure is normalized.

Eclampsia in the 21st century
Michal Fishel Bartal; Baha M. Sibai
Eclampsia is one of the most serious acute complications of pregnancy, and it carries high morbidity and mortality for both the mother and baby. Because it is a rare complication 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.

The Preeclampsia Foundation: the voice and views of the patient and her family
Eleni Z. Tsigas
On the occasion of the Preeclampsia Foundation’s 20th anniversary, we highlight the personal stories of affected patients and their families and raise awareness about the Foundation’s strategies to improve education, healthcare practices, and research for hypertensive disorders of pregnancy.