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ABSTRACT BOOK

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Labor in Gestational Diabetes: INDUCTION

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Gestational Diabetes is one of the most common complications of pregnancy and its incidence is estimated as around 7%. Babies born from women with gestational diabetes (GDM) are significantly more exposed to perinatal risk. This risk is mostly related to foetal macrosomia, associated to increased risk of intrapartum traumatic lesions and asphyxia. The incidence of macrosomia or above 90th percentile birth weight is in fact more common in comparison to general population. Furthermore in GDM pregnancies a C-section increased rate has been observed, mostly unjustified. Pregnancy prolongation beyond 38 weeks increases the risk of foetal macrosomia without reducing C-section rate (2). Because of that, delivery within the 38° week of pregnancy is advisable, if there are not other specific obstetrics recommendations to determine an alternative management. The guidelines in use are mainly based on retrospective studies and experiences of single hospital contexts on maternal and perinatal outcomes though (1). This leads to ample possibilities of variation in the clinical management of these women: expectant, induction or elective C-section. Strong evidence, based on prospective studies and randomized controlled trials, in favour or against the effectiveness and safeness of induction in women with GDM, are missing (3).
Therfore we decided to draw and to manage a Multicenter Randomized Controlled Trial on Induction of labor at 38 weeks versus expectant management in GDM (GINEXMAL).
A total sample of 1760 patients (880 per intervention group) has been planned to be recruited. This power of recruitment will be able to demonstrate a difference between the two arms ≥ 6% (31% of C-section in the expectant group and 25% in the induction group.

At 38+0 -39+0 weeks of gestation, patients eligible to participate in the study will be provided a comprehensive explanation from the

health provider. Patients who will agree to participate will provide written informed consent.

Women recruited will be assigned to:

1) experimental group: induction of labour (38 w+ 0 day – 38 w.+ 6 days);
2) control group: expectant management.

Patients enrolled for the conservative management arm will be followed twice weekly for fetal wellbeing by NST+BPS. Patients will be followed up to 41+0 weeks. Patients who will not deliver until this gestational age will be admitted for labor induction (see above protocol). Induction of labor will be offered when non-reassuring tests for fetal wellbeing are present.

All patients in the conservative arm will undergo US-EFW prior to induction. Patients with EFW>4000g will be offered CS.

Inclusion criteria:

- Maternal age > 18;
- Singleton pregnancy in vertex presentation;
- Gestational age between 38-39 weeks verified by LMP and/or first trimester ultrasound when available;
- Women diagnosed with GDM in the current pregnancy [Diagnosis will be based upon abnormal 50 Gr. GCT (>140) followed by >2 abnormal indices in the OGTT (according to C&C criteria). Women with GCT>200 mg/dl will undergo 100 gr OGTT as well. *If prior to study beginning HAPO consensus will be available, diagnosis of GDM will be based on these criteria*];
- No other contraindication for vaginal delivery.

Exclusion criteria:

- Pre-GDM;
- Prior CS;
- Suspected estimated fetal weight >4000 gr. at enrollment;
- Any known contraindication for vaginal delivery;
- Uncertainty concerning gestational age;
- Non reassuring fetal wellbeing necessitating immediate obstetrical intervention (prompt delivery/prompt CS);
- Maternal complicating pregnancy disease necessitate delivery (e.g Severe PET);

- Women in which Bishop score is >7 at enrollment;
- Known fetal anomaly.

The recruitment begann from June 2010 and it's on going by 6 Centers. More 3 Centers 're waiting the ethical approval of the protocol by their Ethical Committees.

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Continuous insulin infusion systems: benefits and problems

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The achievement of optimal metabolic control during all phases of pregnancies complicated by pre-existent diabetes is now recognized as an essential goal. To minimize risks of adverse pregnancy outcome, near-normal glycemic levels should be obtained and maintained at conception, during embryogenesis, in the central part of gestation, and during labor. In this perspective, great expectations have been placed on the use of continuous subcutaneous insulin infusion (CSII) with micropumps, because of more physiological mode of infusion, miming normal insulin secretion. Micropumps allow a constant and continuous basal infusion of rapid insulin (so solving problems related to the use of long-acting modified molecules), and adjustable boluses. Actually, experiences with CSII outside pregnancy have evidenced clinical advantages over conventional intensified therapy with multiple daily insulin injections (MDI): lower glycemic variability, less frequent hypoglycaemic events, more flexible lifestyle, all resulting in better quality of life.

At the present time, however, clear evidences in favour on CSII during pregnancy are still lacking (1). A few pioneering experiences were conducted in the last decades of the past century, with RCT comparing first-generation pumps with old MDI schemes, still using human insulin (pre-analogues era). No advantages were reported with the new form of treatment, either in term of maternal metabolic control, or regarding pregnancy and perinatal outcome (2-5). We must take into account, however, that these data are hardly transferable to the present situation, where very sophisticated devices and new insulins are used.

After the introduction, in the early 2000, of new-generation pumps, smaller, easier to use, and more versatile, only few articles have been published in this field; most are retrospective or case-control studies. Results on maternal, obstetrical and perinatal outcomes do not differ from those obtained in older trials (6-12); as in non-pregnant population, however, positive effects are reported in glucose

variability and quality of life (13). One of the main limits in achieving real glycemic optimization, leading to normal pregnancy outcome, certainly consists in the fair for hypoglycemia, especially during the night. The recent availability of real-time continuous glucose monitoring and of integrated systems linking glucose sensors and infusion micropumps, with alarms for hypo- and hyperglycaemic excursions, could be very useful in overcoming this impasse. Frequent corrections based on real-time monitoring of glucose concentration could eventually allow well-trained patients to normalize glucose profiles. Although large randomized studies on the use of sensor-augmented CSII in pregnancy are not available, first anecdotic reports on this new therapeutic approach are very encouraging (14).

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GDM: the long term consequences for the fetus

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The epidemic of obesity and type 2 diabetes has major impact on public health and underlines the urgency for identification of risk groups to target preventive strategies. Studies of developmental origins of health and disease have highlighted the possible role of intrauterine exposure to hyperglycaemia as in maternal diabetes in the pathogenesis of overweight, type 2 diabetes and cardiovascular disease [1-3], and maternal hyperglycaemia may also affect offspring cognitive function [4-6].
Our knowledge is primarily based on studies from the Pima Indians from Arizona, US. In this population diabetes in pregnancy as well as 2-hour blood glucose during an oral glucose tolerance test in pregnancy were strong predictors of overweight and type 2 diabetes in the adult offspring [7,8]. Solid data also exist from the North western group in Chicago. Here the offspring of an ethnically mixed group of diabetic women have been followed to the age of 16 years. The main findings were in accordance with the findings in the Pima Indians [9].
This presentation will focus in data from our recent follow-up study of 18-27 year old primarily Caucasians exposed to various degrees of maternal glucose intolerance during pregnancy [10,11]. Our focus was on associations between maternal glucose metabolism during pregnancy and offspring outcome. Data on prevalence, risk estimates and predictors of pre-diabetes/type 2 diabetes, overweight, the metabolic syndrome and offspring cognitive function in the offspring will be presented. We found that offspring of women with diet-treated GDM had an eight-fold higher risk of pre-diabetes/type 2 diabetes, a two-fold higher risk of overweight and a four-fold higher risk of the metabolic syndrome than offspring from the background population. Maternal overweight was the strongest predictor and maternal 2-h glucose was also an independent predictor, whereas birth weight did not predict offspring outcome. Furthermore, the offspring showed impaired cognitive function, but this difference was no longer

significant when adjusted for possible confounders like social class and education.
In summary: offspring of women with diet-treated GDM are at risk of type 2 diabetes, overweight and the metabolic syndrome in adulthood and intrauterine hyperglycaemia may play a role in the pathogenesis. Differences according to cognitive function seemed explained by confounders.

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Obesity and Gestational Diabetes Mellitus

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Obesity and Gestational Diabetes Mellitus (GDM) are interrelated entities.

First, pregestational maternal body mass index (BMI) is a very important risk factor for GDM with OR of 2.14, 3.56 and 8.56 for overweight, obese and severely obese women respectively (Chu 2007).

Second, GDM and pregestational BMI influence common perinatal outcome variables such as macrosomia and cesarean section (Ehrenberg 2004a, Ehrenberg 2004b, Ricart 2005a), the population attributable fractions being higher for BMI than for GDM (Ricart 2005 b). The influence of BMI is also present in outcomes classically linked to maternal diabetes such as congenital malformations (García-Patterson 2004) and neonatal hypoglycemia (García-Patterson 2010).

And last but not least, both conditions are linked to an increased risk of obesity in the progeny, the risk of maternal overweight outweighing the influence of GDM (Pirkola 2010).

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Obstetric Monitoring: new technologies

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Diabetic pregnancies still remain a challenge for modern obstetrics care, in fact diabetes is associated with an increased fetal and neonatal risks, with a four time fold incidence of stillbirth than in general population. Furthermore fetal macrosomia may jeopardize 20% of the diabetic pregnancies. New tests and technologies have been introduced to monitoring the fetal wellbeing and to decrease fetal and neonatal morbidity and mortality. Unfortunately the pathway leading to fetal hypoxia and distress seems to be multifactorial and therefore difficult to completely understood.
Ultrasounds provide an incredible amount of data on fetal monitoring. Starting from the first trimester, high resolution ultrasound probes produce information on fetal morphology, anticipating the second trimester anomaly scan. In addition a computerized nuchal translucency thickness calculation has been proposed for a reliable and easy to perform measurements, indicating a low or high risk pregnancy for congenital heart malformation.
There is a five to eight fold increased risk for congenital malformations and among them the cardiac ones are the most frequent. Ultrasound 3D model reconstructions, with cardio stick, manage to improve the sensitivity and specificity of the detection and diagnosis of these malformations.
Another important issue is fetal growth. Ultrasounds are able to well characterize the fetal biometry of any fetal organs and apparatus. This ability is of fundamental importance for the diagnosis of IUGR or fetal macrosomia. In addiction, ultrasounds may perform fetal weight estimation, which is crucial in order to establish the better route of delivery.
The fetal weight estimation remains one of the biggest challenges in the obstetrics monitoring, with a mean error of 10%, and more relevant errors in case of larger babies. The 3D biometry and the

artificial intelligence, working with inverse neural network, may deliver better fetal weight estimation with an average error of less of 5% in all the study populations.
The new technologies may supply useful information to improve the fetal outcome in case of diabetic pregnancy. The modern obstetricians have to learn and master all these new tools to provide better health care, integrating them in the clinical practice.

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GDM: how to reach a Consensus in Europe

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Gestational diabetes (GDM) occurs when pancreatic function is not sufficient to overcome the insulin resistance created by changes in diabetogenic hormones during pregnancy. The initial criteria for the diagnosis of GDM was established by O'Sullivan and Mahan in 1964 (1). After various modifications, the same criteria remain until now: to identify women at high risk for developing diabetes after pregnancy. The International Association of Diabetes and Pregnancy Study Groups (IADPSG) considers it is more convenient, instead, to identify pregnancies with increased risk for adverse perinatal outcome (2).
The term gestational diabetes has been used to define women with onset or first recognition of abnormal glucose tolerance during pregnancy. However, in 2010, the International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommended a change to this terminology. In this system, diabetes diagnosed during pregnancy is classified as overt or gestational. A diagnosis of overt diabetes can be made in women who meet any of the following criteria at their initial prenatal visit: Fasting plasma glucose ≥126 mg/dL [7.0 mmol/L], or A1C ≥6.5 percent using a standardized assay, or random plasma glucose ≥200 mg/dL [11.1 mmol/]. About 10 percent of women formerly classified as GDM have circulating islet-cell antibodies; these women may have a "latent" form of type 1 diabetes, although their risk of developing type 1 diabetes is not known (3). These women may also comprise a small part of the new overt diabetes classification. Identifying overt diabetes early in pregnancy may be important because these women may be at increased risk of having a child with a congenital anomaly and may be at increased risk of complications from diabetes (nephropathy, retinopathy). Early identification and treatment of hyperglycemia may reduce these risks.

Screening, diagnosis, and treatment of GDM is cost-effective (4). Universal screening is more convenient than selective screening of high risk population. Identification and treatment of gestational hyperglycemia can improve pregnancy outcome; selective screening approaches are cumbersome and not sufficiently sensitive.
The one step approach using a 75 gram two hour oral GTT is superior to the two step 100 gram three hour GTT approach for identifying the pregnancy at risk for adverse outcome. This conclusion is based on results from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Trial, which evaluated about 25000 pregnant women for diabetes using a two hour 75 gram oral GTT (5). The investigators found a continuum of increased risk of adverse outcome when one or more abnormal values were identified (0 hour >92 mg/dL [5.1 mmol/L] and/or 1 hour >180 mg/dL [10 mmol/L] and/or 2 hour >153 mg/dL [8.5 mmol/L]). These adverse outcomes included macrosomia, cesarean delivery, neonatal hypoglycemia, and cord blood C-peptide elevations (6)
The IADPSG defined thresholds for the two hour 75 g GTT based on outcome data reported for the HAPO study (7). These thresholds represent the glucose values at which the odds of infant birth weight, cord C-peptide, and percent body fat >90 percentile in this study were 1.75 times the estimated odds of these outcomes at mean glucose levels, based on fully adjusted logistic regression models. Compared to women in the HAPO study with all glucose values below the thresholds, women who exceeded one or more of these thresholds had two-fold higher frequency of large for gestational age infants and preeclampsia, and >45 percent increase in preterm delivery and primary cesarean delivery.

Therefore, two discrete phases must be considered in diagnosing DM at pregnancy. At first prenatal visit, measuring of fasting plasma glucose, HbA1c or random plasma glucose will allow to identify and to treat, early, overt diabetes. A 2-h 75-g OGTT at 24-28 weeks of pregnancy will make the diagnosis of overt diabetes, GDM, or normal glucose tolerance

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Placental dysfunction in diabetic pregnancy

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Owing to its position the placenta is exposed to metabolic and hormonal diabetes-associated derangements of both mother and fetus, and one can expect some impact of diabetes on the placenta. One of its key functions is to provide the developing fetus with an adequate amount of nutrients, which are derived from the mother. This transport across the placenta has to be carefully regulated, because over- and undersupply may result in fetal growth disturbances.

The Pedersen hypothesis has stimulated much work to understand transplacental transport of glucose. Several glucose transporter isoforms are expressed in the human placenta, of which GLUT1 can be found in all placental cell types. Despite downregulation of GLUT1 expression and translocation into the trophoblast interior by hyperglycemia *in vitro*, *ex vivo* placental perfusion studies failed to find differences in maternal-to-fetal glucose transport of normal and GDM women independent of their treatment modality. *In vitro* glucose uptake into the trophoblast is only reduced at maternal glucose concentrations above 15 mM. This reflects the high capacity of the placental glucose transport system and can explain why molecular changes in GLUT1 do not affect glucose uptake into and transfer across the placenta. Hence, fetal glucose levels will be independent of molecular changes in placental glucose transporters. Rather they depend primarily on maternal glycemia and the maternal-to-fetal glucose gradient, which is driven by fetal glucose metabolism and, hence, by fetal insulin levels. The notion of unchanged transplacental glucose transport in diabetes is also supported by recent data showing similar glucose concentration differences between venous and arterial umbilical cord blood in normal and GDM pregnancies.

About 50-65% of glucose taken up will be metabolized within the placenta and the remainder supplied to the fetus. Maternal diabetes does not redistribute placenta glucose. Placental glucose metabolism

is predominantly anaerobic and the resulting lactate will be released to the maternal and fetal circulation.

Fetal hyperglycemia stimulates placental glycogen synthesis resulting in higher placental glycogen deposition, a common feature of diabetic placentas suggesting a storage function for excess fetal glucose. The endothelial glycogen stores may be utilized for the fetus in a situation of fetal emergency energy demand, e.g. transient hypoglycemia, when lactate rather than glucose would be the outflowing product because of low-level expression of glucose-6-phosphatase.

Collectively, placental glucose transport appears to be flow limited and changes at the transporter level, if at all, will not affect fetal glucose levels. Apart from the elevated glycogen levels associated with maternal diabetes, the placental glucose transport and metabolism system appears to be quite stable.

Strong association of maternal triglycerides with fetal adiposity as well as the finding of increased fatty streak formation in human fetal arteries when the mothers are hypercholesterolemic, has recently sparked interest in placental lipid handling and transport. It has long been known that the placenta stores more triglycerides and phospholipids in diabetes, but the molecular reasons have remained elusive.

The syncytiotrophoblast microvillous membrane represents the placental surface, which is in contact with maternal blood in the intervillous space. At this interface, maternal lipoproteins, or components thereof, will be taken up into the placenta. This will be accomplished either by endocytosis (mainly by low-density lipoprotein; LDL) or after hydrolysis of HDL (high-density lipoprotein) by endothelial lipase (EL) and subsequent uptake of fatty acids or cholesterol-esters.

In GDM placentas some molecular entities participating in lipid transport and metabolism are upregulated. This includes EL, which hydrolyzes phospholipids and triglycerides and thus will increase free fatty acids for uptake into the placenta and potential storage and/or transfer to the fetal circulation. The HDL receptor SR-BI is also upregulated in GDM. Its major function is to facilitate the uptake of HDL-cholesterol into the trophoblast. Phospholipid transfer

protein (PLTP) is another gene, which is upregulated in total placental tissue in GDMs regardless of maternal BMI. PLTP enhances cholesterol efflux to HDL and contributes to HDL remodeling. Its predominant vascular location suggests the diabetes associated changes to occur in the placental endothelial cells. *In vitro* experiments with placental endothelial cells demonstrated the diabetic environment (glucose + insulin) as regulatory factors leading to altered PLTP expression in GDM.

Thus, currently available evidence demonstrates an enhancement of placental lipid metabolism in GDM. It remains to be demonstrated whether this will lead to increased transfer of lipids to the fetus, and whether these placental changes will be associated with the higher fetal adiposity in GDM.

HAPO Study: how to reach a consensus in Italy

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The International Association of Diabetes and Pregnancy Study Groups (IADPSG) has as principal objectives the foster an international approach to enhance the quality of care, to facilitate research and education in the field of diabetes in pregnancy.
On June 11-12, 2008 the IADPSG sponsored an "International Workshop Conference on Gestational Diabetes Diagnosis and Classification" in Pasadena, California, USA. More than 225 conferees from 40 countries reviewed the published results of the Hyperglycemia & Adverse Pregnancy Outcome (HAPO) Study, additional unpublished HAPO Study findings and results of other published and unpublished work that examined associations of maternal glycemia with perinatal and long-term outcomes in offspring. Following the presentation and review of data, conferees held regional caucuses to consider the clinical implications of the large body of information that had been presented. Subsequently, with coordination from the Consensus Panel Steering Committee/Writing Group, the Panel reviewed further HAPO Study results provided by the HAPO Study Data Coordinating Center. Through this process a consensus, recently published, was reached.
This consensus that indicate new diagnostic criteria for Gestational Diabetes was analyzed and accepted in Italy in a National Consensus that was made on the 30 of march 2010.

Eclampsia: new therapeutic approaches

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Pre-eclampsia is a multisystem disorder of unknown cause that is unique to human pregnancy. It is characterised by abnormal vascular response to placentation that is associated with increased systemic vascular resistance, enhanced platelet aggregation, activation of the coagulation system, and endothelial cell dysfunction (1-2). Although the cause of pre-eclampsia remains largely unknown, the leading hypotheses strongly rely on disturbed placental function in early pregnancy. Episodes of placental hypoxia or reperfusion result in oxidative stress, subsequent apoptotic and necrotic disruption of syncytial architecture, and release of various components from the intervillous space into the maternal circulation, stimulating production of inflammatory cytokines. The excessive systemic inflammatory response of pre-eclampsia results in endothelial dysfunction and associated increased vascular reactivity, preceding onset of symptomatic clinical disease (3).
This pathogenesis (called placental preeclampsia) can explain the early onset preeclampsia, typical of the second trimester of the pregnancy.
In the presence of a placenta with an appropriate size for gestational age, predisposing maternal cardiovascular and metabolic syndrome-like disorders (e.g. genetic, diabetes, obesity, diet) might also be able to set off a cascade of placental and systemic inflammation and oxidative stress, resulting in late onset pre-eclampsia (also called maternal preeclampsia)(4).
The same maternal constitutional factors that increase the risk of developing the maternal preeclampsia syndrome also act at the level of early abnormal placentation as mediators of poor implantation/placentation, typical of the early onset preeclampsia (5).
This hypothesis raises the possibility of preventive therapy, prior to pregnancy to improve implantation, and early therapy during the first stage of the placentation.

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Eclampsia: obstetrics aspects

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Recent figures indicate that between 0.5% and 0.75% of pregnant women have pre-existing diabetes (type1 or type 2), while 5% to 10% develop gestational diabetes (GDM).
Insulin resistance, a key mechanism in diabetes, can induce hypertension with mechanism at the cellular, circulatory and neurological level.
Hypertension, generally defined as a blood pressure of at least 140 mmHg (systolic) or at least 90 mmHg (dyastolic) on at least two occasions, affects up to 2-10% of all pregnancies, up to a rate of 20% during the first pregnancy.
Gestational hypertension *(GH)* is defined by developing hypertension without proteinuria after 20 weeks of gestation, with spontaneous remission within 12 weeks after delivery. 50% of women with GH diagnosed between 24-35 weeks develop pre-eclampsia, and the risk of progression is inversely related to gestational age at onset.
Chronic hypertension *(CH)*, if diagnosed in pregnancy, persists after 12 weeks post-partum.
Pre-eclampsia *(PE)* is defined by new hypertension and proteinuria (excretion of 300 mg or more of protein in a 24-hour urine sample) that develops during the pregnancy later than 20 weeks of gestation; in some case it is superimposed on chronic hypertension. **PE** is defined ***severe*** if blood pressure is over 160/110 mmHg.
Eclampsia is defined by PE with seizures.
Any type of hypertension is more frequent in diabetic pregnancies, with a different distribution among various types of diabetes.
Type 1 diabetes is frequently complicated by PE (3-50%). The rate of PE increases with nulliparity, diabetes duration, presence of microvascular complications (particularly pre-pregnancy diabetic nephropaty), pre-existing hypertension and poor glycemic control.
Women with type 2 diabetes have a higher prevalence of CH (12-18%) than control and type 1 diabetic women (2-11%), and a lower

prevalence of PE (3-15%) than type 1 diabetes. CH increases with age and duration of diabetes.
In women with GDM the prevalence of GH is 6.9-28%, CH 1-3% and PE 2.8-6.7%.
Since all types of hypertensive disorders are more common in diabetic pregnant women, measurement of blood pressure and urinary protein is recommended at each prenatal visit to detect the development of GH or PE.
Prenatal outcome worsens when diabetic pregnancy is complicated by hypertensive disorders, particularly PE. Fetal effects of PE are intrauterine growth restriction (rather than macrosomia, the hallmark of diabetic pregnancy), oligohydramnios and abnormal blood flow in maternal and fetal compartments. PE is associated with an increase in primary caeserian section, preterm birth and need for neonatal intensive care. PE may lead to abruptio placentae, fetal death and maternal morbidity (acute renal failure, cerebrovascular and cardiovascular complications, disseminated intravascular coagulation) and death.
Meticulous glucose control is of paramount importance, given that euglycemia might improve the adverse effects of PE.
GH can progress to PE, so any diabetic pregnant woman with hypertension needs to be followed closely, with attention to new onset of symptoms (severe headache, visual change, right upper quadrant or epigastric pain, nausea and vomiting and changes in fetal movements) and regular evaluation of platelet count and liver enzymes for early detection of PE or HELLP Syndrome (Haemolysis, Elevated Liver enzymes, Low Platelet count). Preferred anti-hypertensive medications in pregnancy include methyildopa, long-acting calcium channel blockers and β-adrenergic blockers.
Due to the increased risk of fetal death, fetal surveillance is recommended as soon as the diagnosis of GH or PE is made, and this should continue until delivery. A twice-weekly antenatal testing can be initiated at 32 weeks of gestation (cardiotocography); besides ultrasound scans is important for the evaluation of fetal growth, amniotic fluid and umbilical artery, uterine artery and ductus venosus Doppler.
Timing of delivery should be based on maternal and fetal conditions.

Severe PE needs to be managed aggressively with control of hypertension and magnesium sulfate seizure prophylaxis.
Antenatal corticosteroids for fetal lung maturation are not contraindicated in diabetic pregnant women and should be given to all subjects at risk of delivery at less than 34 weeks of gestation, but should be administered with additional insulin to keep euglycemia.
Since definitive treatment of PE is delivery of the fetus and placenta, preferably vaginally, induction of labour may be warranted. Even with conservative management, induction of labour is considered in cases of 37 weeks or plus gestational age, fetal lung maturity (32-34 weeks gestational age), favourable cervix or maternal or fetal deterioration despite conservative management.
For patients with extreme premature gestational ages (lower than 32 weeks), expectant management can be considered.
Urgent delivery is necessary in case of worsening thrombocytopenia, progressive liver or renal dysfunction, eclampsia or premonitory signs of eclampsia (progression of neurologic symptoms), suspected placental abruption, evidence of severe fetal growth restriction, nonreassuring fetal surveillance or olygohydramnios.
Long-term consequences in women with type 1 diabetes whose pregnancy was complicated by PE or GH are an elevated risk of hypertension later in life and, only for PE, association with nephropathy and CHD.
There are no data about long-term impact of hypertensive disorders in pregnancy in type 2 diabetic women.
Hypertension after GDM is generally described as one of the components of the metabolic syndrome.
Men and women exposed to PE as a fetus and women born small for gestational age have an increased risk of having (or fathering) a future pregnancy that is complicated by PE. These children also have a heightened risk of high blood pressure, features of metabolic syndrome and cardiovascular disease at relative early age.

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Continuous Glucose Monitoring in pregnancy: could be useful?

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A poor glycemic control in diabetic pregnancies is considered one of the causes of abnormal fetal growth. It follows that a good metabolic control is fundamental during this period in order to normalize fetal weight. Major advances in the management of diabetes during pregnancy over the past 50 years have contributed to dramatic reductions in stillbirths and perinatal mortality but have not had a major impact on birth weight, with the risk of macrosomia persistently increased.
Transient periods of hyperglycemia may explain the high incidence of fetal overgrowth in pregnancies complicated by diabetes, and 6-8 glucose level measurements a day often fail to detect any such peaks. The Continuous Glucose Monitoring (CGM) measures glucose in subcutaneous interstitial tissue fluids, enabling glucose levels to be monitored continuously throughout the day and providing useful information on the magnitude and duration of any glucose peaks.
Various published studies have demonstrated the utility of the CGM in monitoring diabetes control during pregnancy. Detailed data on the magnitude and duration of glucose fluctuations, particularly overnight and after meals, give unique insights into daily glycaemic control, which are especially valuable during the physiological changes of pregnancy. Additionally, CGM provides patients with visual feedback on the consequences on glycaemia of factors such as diet, exercise, and insulin regimens, which can be harnessed as a powerful educational tool.
CGM during pregnancy is associated with improved glycaemic control in the third trimester, lower birth weight, and reduced risk of macrosomia. The CGM profiles obtained yielded maximal information about the frequency, magnitude, and duration of glucose excursions. The increased scrutiny of glucose excursions facilitated by CGM may contribute to increased motivation and compliance with

self management. CGM can advance our understanding and classification of normoglycemia during pregnancy.
No studies have considered the potential relationship between the specific glucose variability parameter and fetal growth. Hence it is of interest to investigate the relationship between glycemic profiles detected with the CGM and various fetal growth parameters in type 1 and GDM pregnant women. Using CGM (which can give a more complete picture of the glycemic levels in a pregnant woman during the course of the day), we evaluated several indices of glycemic variability (the MAGE, the mean glycemia value and the M-value) and correlated them with fetal growth.
The CGM disclosed an impaired glucose profile in about 60% of GDM patients, who were consequently given insulin therapy. Glycemic variability, as evaluated by M-value and MAGE, it could be important in determining fetal overgrowth and in diabetic women the second trimester of pregnancy appears to be critical for fetal growth. However we need to be mindful that CGM is still an experimental measure and not a routine clinical tool. The frequency needed for CGM in diabetic pregnancy and its hypothetical advantage over self-monitoring blood glucose in enhancing pregnancy outcome still needs future studies, large enough to provide definitive data.

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