Report of the Canadian Hypertension Society Consensus Conference: 1. Definitions, evaluation and classification of hypertensive disorders in pregnancy

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Abstract

Objectives: To provide Canadian physicians with a standard definition of hypertension in pregnancy, recommendations for laboratory investigations and tests for the assessment and management of hypertensive disorders in pregnancy, and a classification of such disorders.

Options: To improve or not improve Canadian uniformity and standardization in the investigation and classification of hypertensive disorders in pregnancy.

Outcomes: 1) Accuracy, reliability and practicality of diagnostic clinical criteria for hypertensive disorders in pregnancy. 2) Laboratory tests useful to determine severity and prognosis of disorders as measured by maternal and neonatal adverse outcomes. 3) A classification of disorders for use by Canadian physicians to facilitate uniformity and diffusion of research through a common language.

Evidence: Articles on hypertensive disorders in pregnancy published from 1966 to 1996, retrieved through MEDLINE search, related to definitions, tests, diagnostic criteria and classification, as well as documents on diagnosis and classification from authorities in the United States, Europe and Australia and from special interest groups.

Values: High priority was given to the principle of preventing adverse maternal and neonatal outcomes through the provision of diagnostic criteria for severity and prognosis and through dissemination of reliable and pertinent information and research results using a common language.

Benefits, harms and cost: Higher degree of vigilance in diagnosing hypertensive disorders in pregnancy, allowing for earlier assessment and intervention, and more efficient dissemination of comparative information through common language. No harm or added cost is perceived at this time.

Recommendations: (1) A diastolic blood pressure of 90 mm Hg or more should be the criterion for a diagnosis of hypertension in pregnancy and should trigger investigation and management. Except for very high diastolic readings (110 mm Hg or more), all diastolic readings of 90 mm Hg or more should be confirmed after 4 hours. (2) A regularly calibrated mercury sphygmomanometer, with an appropriate-sized cuff, is the instrument of choice. A rest period of 10 minutes should be allowed before taking the blood pressure. The woman should be sitting upright and the cuff positioned at the level of the heart. (3) Both Korotkoff phase IV and V sounds should be recorded, but the phase IV sound should be used for initiating clinical investigation and management. (4) A urine protein level of more than 0.3 g/d should be the criterion for a diagnosis of proteinuria; 24-hour urine collection should be the standard method for determining proteinuria. (5) Edema and weight gain should not be used as diagnostic criteria. (6) Hypertensive disorders diagnosed during pregnancy should be classified as pre-existing hypertension; gestational hypertension with or without proteinuria; pre-existing hypertension with superimposed gestational hypertension with proteinuria; and unclassifiable antenatally but final classification 42 days after delivery.

Validation: Except for expert opinions and reviews solicited for this project, these recommendations need to be field tested and validated in Canada. Guidelines en-

Education

Éducation

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dorsed by the Canadian Hypertension Society and the Society of Obstetricians and Gynaecologists of Canada.
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Résumé

Objectifs : Fournir aux médecins du Canada une définition normalisée de l'hypertension gravidique, des recommandations sur les investigations et les tests de laboratoire servant à évaluer et à traiter les troubles de l'hypertension au cours de la grossesse, ainsi qu'une classification des troubles en question.
Options : Améliorer ou non l'uniformité et la normalisation au Canada de l'investigation et de la classification des troubles de l'hypertension au cours de la grossesse.
Résultats : 1) Exactitude, fiabilité et aspect pratique des critères cliniques permettant de diagnostiquer des troubles de l'hypertension au cours de la grossesse. 2) Tests de laboratoire servant à déterminer la gravité et le pronostic des troubles mesurés par les résultats indésirables chez la mère et le nouveau-né. 3) Classification des troubles que les médecins du Canada pourront utiliser pour faciliter l'uniformité et la diffusion des recherches grâce à une terminologie commune.
Preuves : Articles sur les troubles de l'hypertension au cours de la grossesse publiés entre 1966 et 1996, extraits à la suite d'une recherche dans MEDLINE, portant sur des définitions, des tests, des critères de diagnostic et la classification, et documents sur le diagnostic et la classification provenant d'autorités des États-Unis, de l'Europe et de l'Australie, ainsi que de groupes d'intérêt.
Valeurs : On a accordé une grande priorité au principe de la prévention des résultats indésirables chez la mère et le nouveau-né en fournissant des critères de diagnostic permettant d'établir la gravité et le pronostic et en diffusant des renseignements et des résultats de recherche fiables et pertinents fondés sur une terminologie commune.
Avantages, préjudices et coûts : Plus grande vigilance dans le diagnostic des troubles de l'hypertension au cours de la grossesse, ce qui permet une évaluation et une intervention plus rapides, et diffusion plus efficiente de renseignements comparatifs grâce à une terminologie commune. On ne prévoit aucun préjudice ni coût supplémentaire pour le moment.
Recommandations : 1) Une tension artérielle diastolique de 90 mm Hg ou plus devrait être le critère qui permet de diagnostiquer une hypertension gravidique et devrait déclencher des activités d'investigation et de traitement. Sauf dans le cas des lectures diastoliques plus élevées (110 mm Hg ou plus), toutes les lectures diastoliques de 90 mm Hg ou plus devraient être confirmées après 4 heures. 2) Le sphygmomanomètre au mercure étalonné régulièrement, doté d'un brassard de la bonne grandeur, est l'instrument de choix. Il faudrait prévoir une période de repos de 10 minutes avant de prendre la tension artérielle. La patiente devrait être assise en position verticale et le brassard devrait être placé au niveau du coeur. 3) Il faudrait noter les bruits de Korotkoff des phases IV et V, mais le bruit de la phase IV devrait servir à déclencher l'investigation clinique et le traitement. 4) Un taux de protéines dans l'urine qui dépasse de 0,3 g/j devrait être le critère qui permet de diagnostiquer une protéinurie; la collecte des urines de 24 heures devrait être la façon normalisée de déterminer la protéinurie. 5) L'oedème et le gain de poids ne devraient pas servir de critères de diagnostic. 6) Les troubles de l'hypertension diagnostiqués au cours de la grossesse devraient être classés comme hypertension préalable, hypertension gravidique avec ou sans protéinurie, hypertension préalable conjuguée à une hypertension gravidique avec protéinurie, et hypertension anténatale inclassable, mais classification finale 42 jours après l'accouchement.
Validation : Sauf dans le cas des avis d'experts et des examens sollicités aux fins du présent projet, ces recommandations doivent faire l'objet d'essais pratiques et être validées au Canada. Ce guide a reçu l'aval de la Société canadienne d'hyperthension artérielle et la Société des obstétriciens et gynécologues du Canada.
Commanditaire : La rédaction de ce guide a été financé par la Société canadienne d'hypertension artérielle.

Hypertensive disorders in pregnancy remain a major cause of maternal, fetal and neonatal morbidity and mortality in Canada. An estimated one-third of all maternal deaths in the country are caused by hypertensive disorders, a trend that has changed little since the early 1970s.[1] Pregnant women with hypertension, either newly diagnosed or pre-existing, remain at risk for severe complications such as abruptio placentae, cerebrovascular accident, end-organ failure and disseminated intravascular coagulation.[2–7] As well, the fetus is at risk for intrauterine growth retardation, prematurity and intrauterine death.[2,5,8,9]

Despite recent advances in our understanding of the pathophysiology and control of hypertensive disorders in pregnancy, confusion abounds in the literature regarding the definitions and classifications of such disorders. Terms such as "pre-eclampsia," "gestational hypertension," "toxemia of pregnancy," "proteinuric hypertension," "pre-eclamptic toxemia," "pregnancy-induced hypertension," "organic hypertension," "true pre-eclampsia," "latent essential hypertension in pregnancy," "chronic hypertension" and "transient hypertension in pregnancy" have been used, invariably being misused and interchanged.

If progress in the diagnosis and management of hypertensive disorders in pregnancy is to be facilitated through the dissemination of information between individuals and centres, it is essential that uniform terminology and classification be used. Equally, there should be consensus on how blood pressure should be measured, what constitutes "high" blood pressure and when investigations should be initiated in order to assess possible organ damage and to determine the prognosis for both mother and child. Without such uniformity through consensus, it becomes an onerous task to compare results of studies and share information in a meaningful way.

Although most developed countries have come up with their own classification and definitions, no classification for use in Canada has been proposed to date. Canadian physicians have had to use definitions and classifications developed in the United States,[2,10,11] Europe[12] and Australia[8] or by specialty interest groups.[13–15]

Because of the seriousness of hypertensive disorders in pregnancy and the absence of consensus statements in this country on the diagnosis, assessment and management of these disorders, the Canadian Hypertensive Society (CSH) initiated a project to reach consensus on (a) the definitions and classification of hypertensive disorders in pregnancy, (b) the nonpharmacologic management of such disorders (Sept. 15 issue) and (c) the pharmacologic management of such disorders (Oct. 1 issue). This first article defines what constitutes hypertension in pregnancy, provides the practising physician with guidelines on how to measure a pregnant woman's blood pressure reliably and recommends specific laboratory investigations to be used to determine severity and prognosis.

Methods

Following the decision by the CHS to initiate the consensus project in 1994, the president of the society (S.W.R.) and cochair (R.F.B.) were charged to strike 3 consensus panels. Both of these physicians had participated in earlier CHS consensus conferences. Canadian physicians, obstetricians and internists with interest and expertise in hypertensive disorders in pregnancy were invited to participate in the project. Geographic representation was stressed. A chair and 5 members for each panel were selected, and the panel's progress was reported directly to the CHS chair (S.R.).

For the definitions and classification, the panel chair (M.E.H.) provided the members (R.F.B., J.S., K.W., P.B.) with articles published from 1966 to 1996, retrieved through a MEDLINE search using the MeSH terms "pregnancy" with "hypertension," "classification" and "diagnosis," and asked them to review the existing definitions, classifications and diagnostic tests. All previously released publications issued by international bodies and specialty societies were also reviewed,[2,8,10–13] as well as published opinions of respected American and European experts.[14–17]

A teleconference was held in early 1995 so that the panel members could review and grade the evidence. Pertinent articles were rated according to the methodologic strength of the studies they described (Appendix 1). The levels of evidence used for rating had been used at an earlier CHS consensus conference on the diagnosis and management of hypertension in nonpregnant individuals.[18]

The recommendations were graded according to the level of evidence supporting them (Appendix 1). Grade A recommendations are based on very strong evidence, and grade D recommendations are based on expert opinion, clinical experience and the collective wisdom of the panelists.

A first draft of the recommendations was circulated to selected members of the overall consensus group for review before a 1-day conference in Montreal in June 1995 that was attended by members of the 3 panels and organizers. All the proposed recommendations were carefully discussed during the conference. Recommendations on contentious issues, where the evidence was marginal, were reached by a collective vote of the conference participants. Consensus was defined as 80% or more of the votes in favour of any recommendation.

A revised draft report of the recommendations was circulated to the panelists of the subgroup who could not attend the Montreal conference and to a few other Canadian obstetricians and perinatologists with expertise in

hypertension during pregnancy. A copy of the report was also sent to the chair of the Perinatal Committee of the Society of Obstetricians and Gynaecologists of Canada for comment and for dissemination with members of that committee. In response to these comments and to comments from *CMAJ* peer reviewers, the consensus panelists modified the document during a second teleconference, in October 1996.

Recommendations

A summary of the recommendations regarding the definition of hypertension in pregnancy and the measurement of blood pressure appears in Table 1. The recommendations were based on the analysis that follows.

Definition of hypertension in pregnancy

The definition of hypertension in pregnancy requires clear recommendations. The panelists felt that recommendations should address whether the definition should include blood pressure elevation from first-trimester readings or absolute readings and whether both systolic and diastolic readings should be required or just diastolic readings. They also felt that the recommendations should address the conditions under which blood pressure is measured, how it is measured and which Korotkoff sounds (IV or V) should be used to define diastole.

Blood pressure normally falls in the second trimester, reaching a mean of 15 mm Hg lower than levels before pregnancy. In the third trimester it returns to the prepregnancy levels.[17] This fluctuation occurs in both normotensive and chronically hypertensive women.

Hypertension in pregnancy can be defined on the basis of absolute blood pressure, mean blood pressure or an elevation in blood pressure during the second trimester from a baseline reading in the first trimester.

Using a rise in pressure between trimesters as a criterion for defining hypertension has several major shortcomings. First, a rise of 30 mm Hg in the systolic pressure and of 15 mm Hg in the diastolic pressure is within the normal range of variation in the 3 trimesters, and in one survey was found to occur in more than 70% of primigravida who had no stigma or sequelae of hypertensive disorders in pregnancy.[17] Second, such a criterion requires at least 2 measurements. The conditions under which blood pressure is measured may not be identical each time. This may lead to unreliable comparisons of readings between the trimesters.[14] Finally, an increment rise of 30 mm Hg in systolic pressure and of 15 mm Hg in diastolic pressure was not found to increase the yield of detecting patients with true hypertension when compared with a method that used an absolute blood pressure reading as the sole criterion[19] and has been shown in a prospective cohort Canadian study to have poor sensitivity (7%–55%), variable specificity (69%–99%) and a low positive predictive value (7%–42%) for predicting pre-eclampsia and hence high false-positive rates (60%–90%).[20] Thus, an absolute systolic or diastolic blood pressure reading is the preferred criterion rather than a change in blood pressure between trimesters.

Traditionally, blood pressure readings used to diagnose hypertension in pregnancy were arbitrarily chosen at 140/90 mm Hg. Readings exceeding 140/90 mm Hg, particularly those exceeding 160/110 mm Hg, have been linked with adverse maternal and neonatal outcomes, especially in the presence of new-onset proteinuria.[3,8,21–26] To date, we have been unable to identify a study that describes maternal and perinatal outcomes in a cohort of patients with a systolic blood pressure greater than 140 mm Hg and a diastolic pressure less than 90 mm Hg. In general, the pathophysiology of hypertensive disorders in pregnancy is secondary to vasospasm. Systolic pressure correlates with cardiac output, and diastolic pressure reflects vascular resistance. Systolic pressure, by being a function of the dynamic changes in cardiac output, is subject to marked variations over a short time. Longitudinal studies of gestational hypertension documented low and high cardiac index, high systemic vascular resistance index and normal filling pressures.[27–30]

Although a sustained systolic pressure of 140 mm Hg or greater may be a reasonable level at which to initiate

Table 1: Recommended definitions and diagnostic criteria for hypertensive disorders in pregnancy

Hypertension in pregnancy should be defined as a diastolic blood pressure of 90 mm Hg or more, regardless of the degree of rise in systolic or diastolic blood pressure between visits (grade C recommendation). A systolic blood pressure of 140 mm Hg or more, although not necessarily defining hypertension in pregnancy, warrants close monitoring of the patient and fetus. (Grade B recommendation)
A regularly calibrated mercury sphygmomanometer is the instrument of choice. An appropriate-sized cuff should be used, the length of the cuff should be 1.5 times the circumference of the upper arm. A rest period of 10 minutes should be allowed before taking the blood pressure. The woman should be sitting, and the cuff should be positioned at the level of the heart. (Grade B recommendation)
Except for very high diastolic readings (110 mm Hg or more), measured with the patient sitting upright, all diastolic readings of 90 mm Hg or more should be confirmed after 4 hours. (Grade D recommendation)
Both Korotkoff phase IV and V sounds should be recorded, but the phase IV sound should be used for initiating clinical investigation and management and hence for identifying pregnant women as having hypertension. (Grade C recommendation)
Proteinuria in pregnancy should be defined as urine protein level in excess of 0.3 g/d; 24-hour urine collection should be used to determine proteinuria. (Grade A recommendation)
Edema and weight gain should not be used to define hypertension in pregnancy. (Grade B recommendation)

closer monitoring of the patient and fetus, the diastolic pressure may have to serve as the cornerstone for diagnosis of hypertension in pregnancy.

A mean blood pressure in early pregnancy of more than 85 mm Hg has been shown to be unreliable in predicting subsequent onset of gestational hypertension later in the index pregnancy[9,31–33] and is cumbersome to calculate in a clinical setting.

Using an absolute diastolic pressure of 90 mm Hg or more as the criterion to identify hypertension during pregnancy has several advantages.[34] It is simple, precise and practical. This criterion falls above 3 standard deviations from mean blood pressures in the first and second trimesters, 2 standard deviations in the third trimester and 1.5 standard deviations at term.[33] A diastolic pressure greater than 90 mm Hg represents a point beyond which perinatal mortality is significantly increased.[35] In one study, the reliance on only the diastolic pressure did not significantly reduce the number of patients identified as having hypertension compared with a system that included both the diastolic and systolic pressures (12.7% and 15.9% respectively).[36]

Measurement of blood pressure

In clinical practice it is impossible to ensure ideal conditions all the time for the measurement of blood pressure. Patient anxiety, physical stress, apprehension and excitement cause transient elevations in blood pressure. Hence, it is essential to confirm high readings on 2 occasions. We were unable to find evidence in support of a particular interval for the 2 readings. We agreed that a 4-hour interval, as suggested by the World Health Organization,[13] may be practical and feasible to *rule out* the diagnosis. In some Canadian centres, community-based support has been established that provides monitoring of blood pressure at home. Should such support exist, it is reasonable to have the second measurement recorded at home. One study showed that about 30% of patients found to be hypertensive in the office proved to be normotensive at home.[37] However, if the first diastolic pressure reading is very high (110 mm Hg or more), observing the patient over a 4-hour interval may be ill advised because treatment may be necessary immediately.

The manual mercury sphygmomanometer is the instrument of choice because it is readily available in all clinics and because standards for calibration and use are well established. The use of automated machines is still controversial. Results from recent validation studies of automated instruments in comparison with manual instruments are promising,[38–40] but the automated readings appear to be lower.[38,39]

There is evidence that a pregnant women's blood pressure depends on her posture. Brachial artery blood pressure is highest with the patient sitting upright, intermediate in the supine position and lowest in the left lateral position.[41]

Korotkoff sounds

There is controversy over whether Korotkoff phase IV (muffling) or phase V (disappearance) should be used in defining diastole. Because pregnancy is a hyperkinetic state, the difference between phase IV and V sounds is increased in pregnancy. This is complicated by the conflicting results of studies comparing the phase IV and V sounds to a "gold standard" of intra-arterial measurements.[41–44]

The American College of Obstetricians and Gynecologists previously recommended using the phase V sound to determine diastole,[10] although this recommendation did not appear in the revised bulletin on hypertension in pregnancy.[11] The American Heart Association, the World Health Organization[13] and the International Society for the Study of Hypertension in Pregnancy[12] and some American experts[14,42] recommended using the phase IV sound. The American National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy[2] recommended recording both phase IV and V sounds and to use the latter.

The following observations have to be taken into account:

- The standard deviation for Korotkoff phase V sound in pregnancy is high because of the hyperkinetic state of pregnancy.[42,45]
- The phase V sound may occasionally reach 0,[17] although some surveys have suggested otherwise.[45,46]
- The phase IV sound is subject to a more frequent interobserver and intraobserver variability than the phase V sound.[47]
- The phase IV sound is 5–8 mm Hg higher than the phase V sound,[47] although this difference may be reduced in hypertensive pregnant patients.[48]
- The phase IV sound, by being higher than the phase V sound, may offer a clinically wider margin of safety in identifying pregnant women at risk for complications from hypertensive disorders.
- The literature regarding which sound correlates with better clinical outcomes remains inconclusive.[49]

We therefore recommend that both phase IV and V Korotkoff sounds be recorded. Phase IV, by virtue of its offering a wider margin of safety, should be used for initiating clinical investigation and management and hence for identifying pregnant women as having hypertension (grade C recommendation). The phase V sound should be recorded for ongoing clinical and hemodynamic re-

search. Research in a Canadian setting is needed to determine which of the 2 sounds correlates best with fetal and maternal outcome measures.

Proteinuria

Proteinuria during pregnancy is consistently defined in the literature as the excretion of proteins in urine in excess of 300 mg in 24 hours (0.3 g/d).[2,10–13] The 24-hour urine collection remains the most reliable method of measurement. Commercially available dipsticks permit simple and rapid testing, but the results are unreliable;[14,19,50] positive results (+1 or greater) warrant further evaluation with a 24-hour urine collection, and negative results do not necessarily rule out proteinuria.

Edema and weight gain

Edema and weight gain during pregnancy are clinical signs commonly used to diagnose hypertensive disorders with proteinuria. Unfortunately, there are no standardized methods to quantitate either, let alone to define a significant level. Edema of the face or hands or both was reported in 64% of normotensive patients in the third trimester,[51] and significant edema of the face and hands occurred in 30% of normotensive women whereas up to 40% of women with eclampsia had no edema before the onset of convulsions.[14] A multicentre study showed a negligible effect of edema and weight gain on perinatal morbidity and mortality.[52]

Edema and weight gain should not be used to define hypertensive disorders in pregnancy.

Recommended laboratory investigations

Hypertensive disorders in pregnancy, particularly gestational hypertension (see the next section on classifications) with or without proteinuria, may produce changes

Table 2: Basic laboratory investigations recommended for monitoring patients with hypertension in pregnancy

Laboratory investigation	Grade of recommendation	Rationale
Hemoglobin and hematocrit measurement[2,53,54]	D	Hemoconcentration supports diagnosis of gestational hypertension with or without proteinuria. It indicates severity. Levels may be low in very severe cases because of hemolysis
Platelet count[56–58,62]	C	Low levels (< 100 000 X 10^9/L) may suggest consumption in the microvasculature. Levels correspond to severity and are predictive of recovery rate in postpartum period, especially for women with HELLP syndrome*
Serum aspartate aminotransferase and alanine aminotransferase measurement[5,61]	C	Elevated levels suggest hepatic involvement. Increasing levels suggest worsening severity
Serum lactate dehydrogenase measurement[5,61]	C	Elevated levels associated with hemolysis and hepatic involvement. May reflect severity and may predict potential for recovery postpartum, especially for women with HELLP syndrome
Protein level in 24-hour urine collection[2,4,10,14]	D	Standard to quantitate proteinuria. If in excess of 2 g/d, very close monitoring is warranted. If in excess of 3 g/d, delivery should be considered
Urinalysis[14,19,50]	A	Dipstick test for proteinuria has significant false-positive and false-negative rates. Results should be interpreted taking into account pH, specific gravity, bacterial or leukocyte count, hemoglobin concentration and red blood cell contamination. If dipstick result is positive (≥ +1), 24-hour urine collection is needed to confirm proteinuria. Negative dipstick results do not rule out proteinuria, especially if diastolic pressure is greater than 90 mm Hg
Serum uric acid measurement[60,72,73]	B	Elevated levels aid in differential diagnosis of gestational hypertension and may reflect severity
Serum creatinine measurement[74]	C	Levels drop in pregnancy. Elevated levels suggest increasing severity of hypertension. assessment of 24-hour creatinine clearance may be necessary. Elevated levels may be within normal limits for nonpregnant people
Fetal assessment		See text for comments
Non-stress test[76–79]	D	
Biophysical profile[80,81]	C	
Fetal movement count[75]	D	
Doppler flow velicitometry[82–86]	B	

*HELLP = Hemolysis, Elevated Liver enzyme levels and Low Platelet count.

in the hematologic, renal and liver profiles that may adversely affect prognosis and both neonatal and maternal outcomes.

In the absence of hemolysis, hematocrit and hemoglobin are measures of hemoconcentration. The volume expansion observed in normal pregnancy is reduced in gestational hypertension,[53] and the degree of intravascular volume depletion depends on the severity of the gestational hypertension.[2]

Compared with normal pregnancies, those complicated by hypertensive disorders show an increased incidence of dysmorphic red blood cells.[54]

Thrombocytopenia occurs in one-fifth of patients with hypertensive disorders in pregnancy[55–57] and is secondary to consumption with endothelial damage, reduced synthesis or destruction by immunologic mechanisms.[58] The combination of elevated liver enzyme levels, hemolysis and thrombocytopenia defines a severe form of gestational hypertension: the HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome.[59] Although thrombocytopenia is a poor predictor of severe disease, it is a useful indicator of severity and potential for recovery.[60–62]

Abnormal liver enzyme levels are associated with gestational hypertension. Elevated levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH) occur as a result of periportal hemorrhagic necrosis. Involvement of the liver is frequently accompanied by involvement of other organs, including the kidneys, and the brain.[5] In the HELLP syndrome, lactate dehydrogenase and thrombocytopenia are measures of severity and potential for recovery in the postpartum period.[61]

The level of fibrin degradation products (FDP) and fibrinogen as well as the prothrombin and partial thromboplastin times may be abnormal to variable degrees, although they remain normal in many patients with hypertension.[63–65] They are not necessarily reflective of severity and hence are of little use for routine screening in gestational hypertension. However, if surgery is being considered in the presence of clinical disseminated intravascular coagulation, it may be advisable to measure the prothrombin and partial thromboplastin times.

Antithrombin III, a glucoprotein synthesized by the liver, is a serine protease inhibitor of thrombin, factor VII and factor Xa. Levels are typically decreased in patients with gestational hypertension and seem to stay normal in those with pre-existing hypertension.[66] The levels appear to correlate inversely with the degree of proteinuria and

Table 3: Proposed classification of hypertensive disorders in pregnancy

Classification	Definition
A. **Pre-existing hypertension**	Diastolic hypertension (as defined in Table 1) that predates pregnancy or is diagnosed before 20 weeks' gestation. In most cases hypertension persists > 42 d post partum. It may be associated with proteinuria.
1. Essential	Primary
2. Secondary	Secondary to such conditions as renal disease, pheochromocytoma and Cushing syndrome
B. **Gestational hypertension**	Diastolic hypertension develops after 20 weeks' gestation. In most cases it resolves < 42 d postpartum
1. Without proteinuria	Corresponds to previous terminology such as "pregnancy-induced hypertension," "transient hypertension" and "nonproteinuric hypertension." Protein excretion in 24-hour urine collection is < 0.3 g/d
a. Without adverse conditions	
b. With adverse conditions	Convulsions (eclampsia); very high diastolic pressure (> 110 mm Hg); thrombocytopenia (platelet count < 100 000 X 10^9/L); oliguria (< 500 mL/d); pulmonary edema; elevated liver enzyme levels; severe nausea and vomiting, frontal headache, visual disturbances, persistent abdominal pain in right upper quadrant, chest pain or shortness of breath; suspected abruptio placentae; HELLP syndrome; intrauterine growth retardation, oligohydramnios, or absent or reversed umbilical artery end diastolic flow, as determined by Doppler velicitometry
2. With proteinuria	Corresponds to previous terminology such as "pre-eclampsia," "pre-eclamptic toxemia" and "toxemia." Protein excretion in 24-hour urine collection is ≥ 0.3 g/d
a. Without adverse conditions	
b. With adverse conditions	Same conditions as in 1b; protein excretion > 3 g/d in 24-h urine collection, especially with hypoalbuminemia (albumin level < 18 g/L)
C. **Pre-existing hypertension + superimposed gestational hypertension with proteinuria**	Pre-existing hypertension (as defined in A) associated with further worsening of blood pressure and protein excretion ≥ 3 g/d in 24-h urine collection after 20 weeks' gestation. Corresponds to previous terminology "chronic hypertension with superimposed pre-eclampsia"
D. **Unclassifiable antenatally**	Hypertension with or without systemic manifestations if blood pressure was first recorded after 20 weeks' gestation. Reassessment is necessary at or after 42 d post partum. If the hypertension has resolved by then, the condition should be reclassified as gestational hypertension with or without proteinuria; if the hypertension has not resolved by then, the condition should be reclassified as pre-existing hypertension

with the severity of maternal morbidity in gestational hypertension.[67,68] Measurement of antithrombin III is of little benefit at present in the clinical management of gestational hypertension. The plasma D-dimer level, fibrinopeptide A level, factor VIII antigen/activity ratio and antithrombin III–thrombin complex levels seem also to correlate with disease severity, but their role in managing hypertensive disorders in pregnancy is still uncertain.[69–71]

How severe should proteinuria be to warrant intervention? The National High Blood Pressure Education Program Working Group[2] suggested a urine protein level of 2 g/d. Other authorities[10,14] suggested 4 to 5 g/d. None of these levels had been objectively assessed to correlate with maternal or perinatal morbidity. It is clear, however, that the disease complex may deteriorate rapidly. With associated hypoalbuminemia, the risk of pulmonary edema is high. Protein excretion of 2 to 3 g/d warrants close monitoring, with serious consideration given to delivery. Microalbuminuria late in the postpartum period seems to be predictive of chronic hypertension 7 years after the pregnancy.[4]

The serum uric acid concentration is an indicator of severity[72] but is a poor predictor of clinically apparent gestational hypertension because the levels rise only within days of the manifestation of the disease.[60] Hyperuricemia in gestational hypertension is associated with intrauterine growth retardation, fetal distress and perinatal loss.[73] Caution should be taken in interpreting serum uric acid levels in pregnancy because of a diurnal variation in the concentration.[73]

Table 4: Definitions related to hypertensive disorders in pregnancy and diagnostic criteria recommended by the Canadian Hypertension Society (CHS) and other international bodies*

Definition/criterion	CHS	NHBPEPWG	WHO	ISSH	ASSH	ACOG
Hypertension, mm Hg	Diastolic pressure (DP) ≥ 90	Blood pressure (BP) ≥ 140/90 **or** rise in systolic pressure (SP) of ≥ 30 and in DP of ≥ 15	DP ≥ 90	DP ≥ 90	DP ≥ 90 and/or SP ≥ 140, **or** rise in SP of ≥ 25 and in DP of ≥ 15	DP ≥ 90 **or** SP ≥ 140
Severe hypertension, mm Hg	DP ≥ 110	DP ≥ 110 or SP ≥ 160	DP ≥ 110 SP ≥ 160	DP ≥ 110	DP ≥ 110 and/or SP ≥ 170	DP ≥ 110 SP ≥ 160–180
Korotkoff sound	IV	V	IV	IV	IV	–
Severe proteinuria (protein excretion in 24-hour urine collection, g/d)	≥ 3	≥ 2	–	≥ 3	≥ 0.3 **or** positive dipstick result of ≥ 2+	> 5

*NHBEPWG = National High Blood Pressure Education Program Working Group (US), WHO = World Health Organization, ISSH = International Society for Study of Hypertension, ASSH = Australian Society for Study of Hypertension, ACOG = American College of Obstetricians and Gynecologists.

Table 5: Classifications of hypertensive disorders in pregnancy proposed by the CHS and other international bodies

CHS	NHBPEPWG	WHO	ISSH	ASSH	ACOG
Pre-existing hypertension (HT), essential/secondary	Chronic HT	Pre-existing HT, renal HT and/or proteinuria in pregnancy; underlying HT or renal disease	Chronic HT Chronic renal disease	Chronic HT, essential/ secondary	Chronic HT
Gestational HT without proteinuria, with or without adverse conditions	Transient HT	Gestational HT Gestational proteinuria	Gestational HT Gestational proteinuria	–	Pregnancy-induced HT (includes pre-eclampsia, eclampsia and HELLP syndrome)
Gestational HT with proteinuria, with or without adverse conditions	Pre-eclampsia/ eclampsia	Pre-eclampsia/ eclampsia	Gestational proteinuric HT	Pre-eclampsia, mild/severe	–
Pre-existing HT + superimposed gestational HT with proteinuria	Pre-eclampsia superimposed on chronic HT	Superimposed pre-eclampsia	Chronic HT with superimposed pre-eclampsia	Pre-eclampsia superimposed on chronic HT	Chronic HT with superimposed pregnancy-induced HT
Unclassifiable antenatally	–	Unclassifiable	–	–	–

Serum creatinine levels fall during pregnancy. Elevated levels, which could be within normal limits for nonpregnant women, occur late in gestational hypertension with proteinuria and are associated with reduction of renal perfusion and glomerular filtration rates. Elevated serum creatinine levels and reduced glomerular filtration rates are associated with severe cases and may represent intrinsic renal changes.[74]

Several tests for assessing fetal well-being have been used. Having the patient record the number of fetal movements periodically on a sheet does not significantly decrease the risk of intrauterine death compared with a policy of asking the patient about fetal movements.[75] In 4 randomized controlled trials, non-stress cardiotocography (measurement of fetal heart rate accelerations corresponding to fetal movements over a 20-minute period) was found to be beneficial in high-risk pregnancies identified as being at risk for fetal death (where perinatal mortality exceeds 15 per 1000 pregnancies).[76–79] The biophysical profile (ultrasound assessment of amniotic fluid volume, fetal movements, fetal tone and fetal breathing) has good predictive properties for fetal morbidity and mortality in high-risk pregnancies.[80,81] Doppler umbilical blood flow analysis in high-risk pregnancies has been predictive of perinatal morbidity and mortality and has been associated with a decreased risk of emergency cesarean section, antenatal and intrapartum fetal distress and admission to the neonatal intensive care unit.[82–86]

A list of basic investigations and the rationale for their use are presented in Table 2. These tests can be repeated periodically, depending on maternal and fetal status following the onset of the hypertensive disorder.

Classification of hypertensive disorders in pregnancy

Our consensus group reviewed classifications suggested by various international bodies and societies.[2,8,10–15] Our proposed classification, based on our current understanding of the pathophysiology and prognosis for mother and child, is shown in Table 3. We considered issues of feasibility and acceptability by Canadian health care workers. Our classification provides a template for a common language and sets the stages for proper evaluation of outcomes.

Validation

This is the first report from a Canadian consensus group on the definition, assessment and classification of hypertensive disorders in pregnancy. It is hoped that this document will facilitate communication between clinicians and researchers in Canada and abroad.

These recommendations are somewhat similar to those issued by authorities elsewhere (Tables 4 and 5). The nomenclature is altered, but the classification in principle and recommended tests correspond well to those produced by the National High Blood Pressure Education Program Working Group.[4] Our recommendations do differ in that they rely mainly on the diastolic blood pressure to define hypertension in pregnancy and on the Korotkoff phase IV sound to trigger close monitoring and investigation. This latter aspect has been recommended by European and Australian consensus groups and some American authorities.

It is unfortunate that much of the CHS recommendations are based on borderline evidence (mostly grade C and D recommendations [Appendix 1]). Most of the evidence on diagnostic measures came from observational studies, with occasional outcome studies comparing cohorts with hypertensive disorders and those without such disorders. Studies using independent interpretation of test procedures or diagnostic standards are rare. Research is needed to assess the effectiveness of diagnostic tests in predicting disease severity and determining prognosis of maternal and neonatal outcomes.

The CHS recommendations need to be field tested and validated in Canada. These recommendations will be subject to change as new evidence emerges and therefore should be reviewed periodically. Compliance, feasibility and usefulness need to be determined but can be assessed only once these recommendations have been introduced.

The recommendations have been endorsed by the CHS and the Society of Obstetricians and Gynaecologists of Canada.

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Appendix 1: Levels of evidence used by CHS consensus group to rate studies on hypertensive disorders in pregnancy relating to diagnosis and prognosis and to grade recommendations*

Levels of evidence for rating studies of diagnosis

I. (a) Independent interpretation of test procedure (without knowledge of result of diagnostic standard)
   (b) Independent interpretation of diagnostic standard (without knowledge of result of test procedure)
   (c) Selection of patients or subjects who are suspected but not known to have the disorder of interest
   (d) Reproducible description of both the test and the diagnostic standard
   (e) At least 50 patients with and 50 without the disorder
II. Meets 4 of the criteria in I
III. Meets 3 of the criteria in I
IV. Meets 2 of the criteria in I
V. Meets 1 of the criteria in I
VI. Meets none of the criteria in I

Levels of evidence for rating studies of prognosis

I. (a) Inception cohort
   (b) Reproducible inclusion and exclusion criteria
   (c) Follow-up of at least 80% of subjects
   (d) Statistical adjustment for extraneous prognostic factors (confounders)
   (e) Reproducible descriptions of outcome measures
II. Inception cohort but meets only 3 of the other criteria in I
III. Inception cohort but meets only 2 of the other criteria in I
IV. Inception cohort but meets only 1 of the other criteria in I
V. Inception cohort but meets none of the other criteria in I
VI. Meets none of the criteria in I

Grading system for recommendations

A. The recommendation is based on 1 or more studies at level I
B. The best evidence available was at level II
C. The best evidence available was at level III
D. The best evidence available was lower than level III and included expert opinion

*Taken from Carruthers et al,[18] with permission.