Scottish Obstetric Guidelines and Audit Project

A Guideline Development Project initiated by the Scottish Executive Committee of the RCOG, funded by the Clinical Resource and Audit Group of the SODoH and working to the methodology of the Scottish Intercollegiate Guidelines Network

The Management of Mild, Non-proteinuric Hypertension in Pregnancy

A Clinical Practice Guideline for Professionals involved in Maternity Care in Scotland

Pilot Edition

Guideline produced in October 1997 and valid until October 1999

C O N T E N T S

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1 INTRODUCTION

1.1 WHY A CLINICAL PRACTICE GUIDELINE ON THE MANAGEMENT OF MILD, NON-PROTEINURIC HYPERTENSION IN PREGNANCY?

Hypertensive disorders of pregnancy continue to comprise one of the principal causes of maternal death in the UK, ranking second to thrombo-embolism as a cause of direct maternal death in the three most recent triennial reports[1]. Hypertensive disorders are also acknowledged to be associated with increased risks of stillbirth and neonatal death. Proteinuric pre-eclampsia has been reported to carry a relative risk of 9.6 for stillbirth (and diastolic hypertension alone, a relative risk of 4.1) compared with normotensive women.[2]

Data from the England, Wales and N.Ireland Confidential Enquiry into Stillbirths and Deaths in Infancy (CESDI), 1994, suggest that 4.7% of such deaths are attributable to hypertensive disorders[3] and equivalent Scottish data[4] attribute 6% of perinatal mortality to hypertensive disease.

The Reports of the Confidential Enquiry into Maternal Deaths [1] have repeatedly highlighted the need for clear guidelines for the management of severe hypertensive disorders and there is increasing awareness of appropriate drug treatments for severe pre-eclampsia and eclampsia. Suitable protocols, based on national recommendations, for the management of women with proteinuric pre-eclampsia should already be in place in Scottish maternity units.

Less attention has been paid to the management of mild, non-proteinuric hypertension in pregnancy. There is confusion about the relationships between various categories of mild disease and about their clinical implications and potential to progress to severe disease. In view of these confusions, it was felt appropriate to include the management of the mild hypertensive disorders among the first four topics to be addressed by SOGAP.

It is hoped that this guideline will aid appropriate management of patients with non-proteinuric hypertension (approximately 10% of all antenatal patients). Use of the guideline should reduce unnecessary hospital admissions and over-investigation of this patient group and will, hopefully, lead to a more cost-effective pattern of care while minimising disruption to the lives of patients and their families.

1.2 WHO HAS DEVELOPED THIS GUIDELINE

This Guideline has been developed by a multi-professional working group representing teaching hospitals, district general hospitals and primary/community care settings. The group was convened by the grant holders of the Scottish Obstetric Guidelines and Audit Project (SOGAP). The views of patients have been sought by review of an advanced draft of this document by a representative of Action on Pre-eclampsia (APEC). The SOGAP project was originally conceived, and the topics for guideline development chosen, by the Scottish Executive Committee of the RCOG with input from the funding body, the Clinical Resource and Audit Group (CRAG) of the SODoH.

1.3 FOR WHOM IS THIS GUIDELINE INTENDED?

The guideline has been produced under the auspices of the Scottish Executive Committee of the RCOG and is aimed at all healthcare professionals who share in the provision of antenatal care. In particular, it is hoped that fellows, members and diplomates of the RCOG and their trainees, general practitioners and midwives will find it helpful.

1.4 WHAT METHODS HAVE BEEN USED IN THE DEVELOPMENT OF THIS GUIDELINE

The development of the guideline has drawn on methodology outlined in the CRAG publication *'Clinical Guidelines'*[5], the SIGN publication '*Clinical Guidelines: Criteria for Appraisal for National Use*'[6] and the NHS Executive's '*Clinical Guidelines*'[7].

In preparing the Guideline, a systematic literature search was undertaken using *CD plus Medline* for the years 1986 - 1996 (principal search terms: hypertension and pregnancy) and the C*ochrane Pregnancy and Childbirth Database (CPCD)* in order to identify evidence from randomised controlled trials (RCTs), other forms of clinical study and expert opinion which is appropriate for translation into clinical practice in Scotland. Material identified through the searches was supplemented by references already known to group members and by scrutiny of the reference lists of identified publications for key references from earlier years.

The guideline development group particularly acknowledges the content of the US National High Blood Pressure Education Program Working Group Report on High Blood Pressure in Pregnancy[8] and the WHO Technical Report (no. 758) on the hypertensive disorders of pregnancy[9] and has drawn on these documents in the preparation of this guideline.

The recommendations within this guideline have been graded according to the levels of evidence on which they are based, using the scheme adopted by SIGN[6] which is based on the system proposed by the US Agency for Health Care Policy and Research (AHCPR)[10]. The scheme for grading of recommendations is reproduced here (Table I).

The guideline development group met on three occasions and developed successive drafts of the guideline. An advanced draft was then submitted for peer review to a panel of two Scottish obstetricians plus nominees of the RCGP and RCM who had not been involved in the development process. The suggestions of the peer reviewers and of a consumer representative were incorporated prior to submission of an advanced draft to the SIGN editorial board and the Scottish Executive Committee of the RCOG.

Minutes of the guideline development process and copies of all publications quoted in the text are held at the SOGAP offices in Glasgow and Aberdeen.

Table I Grading of recommendations

Grade	**Recommendation** (based on AHCPR 1994)
A	Requires at least one randomised controlled trial as part of the body literature of overall good quality and consistency addressing the specific recommendation
B	Requires availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation
C	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.

Throughout the text of the guideline, it has been made explicit which individual recommendations are based on evidence from RCTs (Grade A recommendations), other designs of clinical studies (Grade B recommendations) or on the consensus view of the Guideline Development Group, indicating an absence of relevant studies, (Grade C recommendations).

Grade A recommendations (those based on evidence from RCTs) are highlighted by means of a shaded text throughout.

1.5 HOW WILL THIS GUIDELINE BE IMPLEMENTED AND REVIEWED?

This guideline was launched, along with three other guidelines being developed by SOGAP, at a national meeting in March 1997 to which representatives of key disciplines from throughout Scotland were invited. Discussion of the guideline in this forum allowed minor modifications to be made in the light of suggestions from a wider group. A lead clinician from each maternity unit in Scotland will be recruited to initiate the development of local protocols based on the four SOGAP guidelines. Local protocol development and implementation will be supported by site visits by the SOGAP team during the final year of the project timetable.

The impact of the SOGAP guidelines on the process and outcome of care will be monitored through the project's audit component. A profile of pre-guideline practice based on the results of a questionnaire survey of relevant professional groups (to assess the process of care), and on analysis of relevant data collected by the Information and Statistics Division (ISD) of the NHS in Scotland (to assess the outcome of care), is enclosed with this document. In due course, a similar profile of post-guideline practice will be compiled, using the same methods, in order that any changes can be identified.

In addition to the audit component described here, it is suggested that clinicians might include audit of compliance with this guideline in local audit programmes. A suggested minimum data set which might be used for this purpose is included in this document (Appendix I).

This guideline is based on evidence and consensus views available at the time of final preparation (October 1997) and will be reviewed under the direction of the Scottish Executive Committee of the RCOG in October 1999, or sooner if changing evidence requires it.

1.6 DECLARATION OF INTERESTS

Declarations of interests (personal, specific and non-specific; non-personal, specific and non-specific) as defined by SIGN[7] have been obtained from all Guideline Development Group members. No conflicts of interest have been identified and copies of all declarations are held at the SOGAP offices in Glasgow and Aberdeen.

2. THE GUIDELINE

2.1 DEFINITIONS AND CLASSIFICATION

Recommendations

- The classification of the hypertensive disorders of pregnancy used should be the ISSHP classification (Davey and MacGillivray, 1988).
(**GRADE C**)

- The diagnosis and nomenclature of the hypertensive disorders of pregnancy should be based on the definitions of *hypertension* and *proteinuria* used in the ISSHP system.
(**GRADE C**)

- In measuring blood pressure, appropriate, well-maintained equipment should be used with a sphygmomanometer cuff size appropriate for arm size.
(**GRADE B**)

- Blood pressure should be measured with the woman's arm resting at heart level.
(**GRADE B**)

- Diastolic pressure should be recorded as Point IV Korotkoff (ie the point where muffling of sounds occurs).
(**GRADE C**)

- The diagnosis of proteinuria can be based on reagent stick testing. Confirmation of positve reagent stick results requires the use of "Multistix" which permit estimation of urinary specific gravity (SG) and pH in addition to protein content.
(**GRADE B**)

Classification

More than 100 names have been used in the English and German literature to describe the hypertensive disorders of pregnancy - and there have been almost as many classifications[11]! The confusion surrounding definition and classification is compounded by the fact that the true diagnosis in cases of hypertension in pregnancy can often be reached only retrospectively, once it is known whether or not the hypertension resolves in the puerperium.

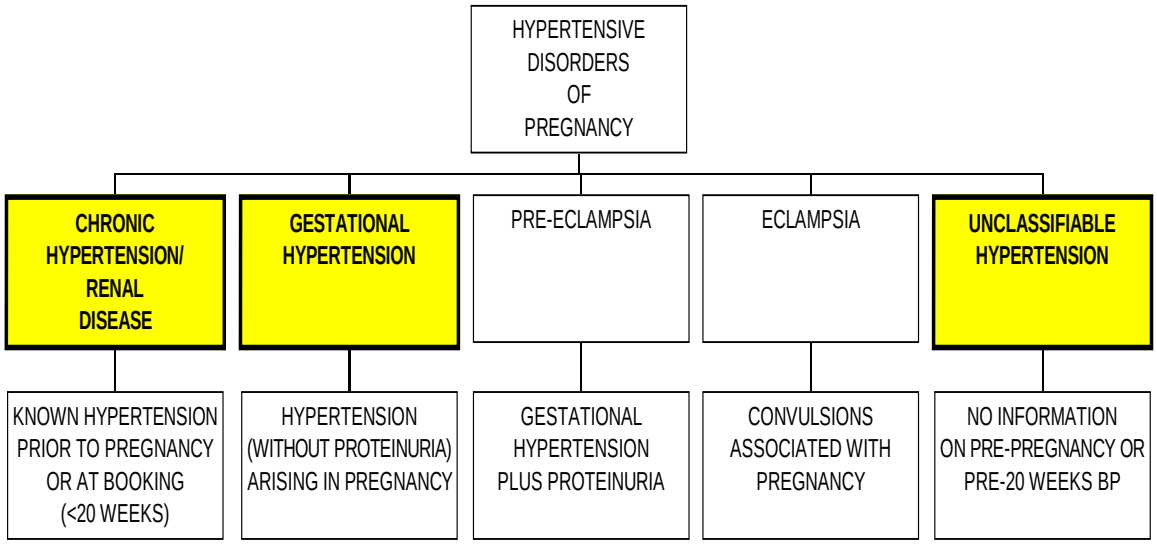
A widely accepted, and relatively simple, classification is that of Davey and MacGillivray[12] which was endorsed by the International Society for the Study of Hypertension in Pregnancy (ISSHP) in 1986. This classification is based on only two clinical features: absolute level of diastolic blood pressure and proteinuria. The definitions of "*hypertension*" and "*proteinuria*" on which this classification is based are reproduced in Table II and the nomenclature to be applied is summarised (in simplified form) in Figure 1.

Table II Definitions of "*hypertension*" and "*proteinuria*" used in the ISSHP classification

1. HYPERTENSION	A Diastolic BP of ≥110mmHg on any one occasion **OR** B Diastolic BP of ≥90mmHg on any two or more consecutive occasions ≥ 4 hours apart.*
2. SEVERE HYPERTENSION	A Diastolic BP ≥ 120mmHg on any one occasion **OR** B Diastolic BP ≥ 110mmHg on two or more consecutive occasions ≥ 4 hours apart.
3. PROTEINURIA	A One 24 hour urine collection with a total protein excretion of ≥ 300mg/24 hrs. **OR** B Two "clean-catch" midstream or catheter specimens of urine (collected ≥ 4 hours apart) with ≥ "++" protein on reagent strip testing. **OR** with ≥ "+" protein **IF** Urine SG <1.030 **AND** pH ≤ 8

* The diagnosis of *hypertension* cannot be made unless the elevated BP has been sustained for at least 4 hours. However, if an elevated diastolic is observed to fall below 90mmHg within a period of <4 hours, then the hypertension can be regarded as "spurious" and the woman need not be detained for further observation.

FIG 1. Summary of the ISSHP Classification (Davey & MacGillivray 1988)



The shaded boxes are those which are discussed within the scope of this Guideline

The ISSHP classification shares many **similarities** with the most widely used alternative, the ACOG (1972) classification[13]. The fundamental similarities between the two classifications are:
1) the distinction between *gestational hypertension* (hypertension developing during pregnancy or the immediate puerperium and regressing after delivery) and *chronic* (or pre-existing) *hypertension*, and 2) the reservation of the term *pre-eclampsia* for gestational hypertension **plus** additional features (which must include proteinuria in the ISSHP classification but may comprise oedema alone in the ACOG).

The fundamental **difference** between the two classifications is that the ISSHP uses a simple definition of *hypertension* (based on an absolute level of diastolic BP of $\geq$ 90mmHg) whereas the ACOG uses an expanded definition of *hypertension* (encompassing a systolic pressure of $\geq$ 140mmHg, an increment in systolic pressure of $\geq$ 30mmHg, an increment in diastolic pressure of $\geq$ 15mmHg and also absolute level and increment criteria relating to *mean arterial pressure* as alternatives to an absolute level of diastolic pressure of $\geq$ 90mmHg).

The SOGAP group favour the ISSHP classification on account of its simplicity and familiarity to UK clinicians. In justifying basing the diagnosis of "hypertension" on diastolic BP only, Davey and MacGillivray[12] quote the work of Friedman and Neff[2] which indicates that the level of systolic BP "does not add to the diagnostic or prognostic significance of the hypertensive disorders of pregnancy".

Blood Pressure Measurement

The US Consensus Report[8] includes an appendix on blood pressure measurement which draws on 1987 recommendations from the American Heart Association (AHA) and from the WHO Study Group on The Hypertensive Disorders of Pregnancy[9]. The AHA have subsequently produced an up-dated report on *Human Blood Pressure Determination by Sphygmomanometry*[14] which includes a section on pregnant patients. The principal recommendations drawn from these documents relating to technical aspects of blood pressure recording are summarised in Table III.

Table III

Recommendations relating to the measurement of blood pressure (drawn from US National High Blood Pressure Working Group Consensus Report[8], WHO Study Group Report[9] and AHA Special Report[14]).
1. A **bell** stethescope should be used for auscultation as it better amplifies the Korotkoff sounds.
2. A **mercury** manometer rather than aneroid sphygmomanometer should be used for preference. All sphygmomanometers should be regularly maintained. In particular, when aneroid instruments are used they should be regularly checked for accuracy against a standard mercury instrument.
3. Clinicians should have access to a range of sphygmomanometer **cuff sizes**. Too small a cuff size will result in over-estimation of blood pressure and too large a cuff, in under-estimation (though to a lesser extent). Ideally, the bladder length should encompass 80% of the arm circumference and the bladder width should be 40% of the arm circumference.
4. Ideally, measurements should be taken with the woman **sitting** after a period of rest and with the arm supported **at heart level**. Measurements are little altered if the woman is lying with lateral tilt as long as the arm is similarly at heart level.
5. During first inflation of the cuff, an approximation of systolic pressure should be obtained by **palpation** of the radial pulse.
6. During auscultation, the cuff should initially be inflated to approximately 20mmHg higher than the approximate systolic pressure determined by palpation. Systolic pressure is then recorded as the level at which repetetive sounds are first heard (Korotkoff I) (rounded, upwards, to the nearest 2mmHg).
7. The diastolic pressure is recorded at the point of muffling of these sounds (Korotkoff IV) (see below), similarly rounded to the nearest 2mmHg

Korotkoff Phases

All documents on the measurement of blood pressure in pregnancy continue the debate as to whether diastolic blood pressure should be recorded at Korotkoff phase IV (muffling of sounds) or V (disappearance of sounds). Davey and MacGillivray advocated phase IV in the ISSHP classification[12] as do the WHO Study Group[9]. The US groups[8,14] favour recording both phases IV and V on all occasions in pregnancy.

After full consideration, the SOGAP group continue to advocate the use of phase IV in routine practice. Since the group is advocating the use of the ISHHP classification, it seems logical also to advocate the technique of blood pressure measurement on which this classification is based. In justifying the choice of a Korotkoff Phase IV reading of 90 mmHg as the cut-off for diagnosing hypertension in pregnancy, Davey and MacGillivray quote earlier work demonstrating that perinatal mortality is significantly increased when blood pressure exceeds this level.

More recently, Lopez et al[15] have conducted a rigorous comparison of the two Korotkoff phases based on numerous recordings in 1194 primigravidae. Contrary to previous reports (based on much smaller numbers), they found that the use of phase V resulted in a very low percentage of "zero" recordings (<0.5%) and that phase V values showed a better association with outcome variables such as proteinuria, IUGR and hyperuricaemia. These authors point out that use of phase IV results in twice as many women being classified as "hypertensive" compared to use of phase V. Thus, phase IV results in lower specificity but higher sensitivity than phase V. A recent editorial by de Swiet and Shennan[16] has also advocated a switch to Korotkoff V.

The group acknowledges that use of phase IV may result in "over-diagnosis" of gestational hypertension. However, this "over-diagnosis" is not felt to be a problem as the management strategies advocated within this guideline for women with mild gestational hypertension are conservative and do not expose women to unnecessary intervention. This issue will be kept under review and may be altered in future editions of this guideline.

Electronic devices for Measuring Blood Pressure

As discussed above, available recommendations suggest that blood pressure in pregnancy is measured using a standard mercury sphygmomanometer. Greer, in 1993[17], and Franx *et al*, in 1994[18] have reviewed the use of various automated devices for the measurement of blood pressure in pregnant women. Both sets of authors concluded that automated devices give readings for diastolic blood pressure which are closer to Korotkoff V than IV. Franx *et al* express great concern about the diastolic measurement error of automated devices and both papers comment that established relationships between blood pressure and feto-maternal outcomes are based on the use of conventional mercury sphygmomanometers. Currently, therefore (particularly in the light of the recommendation to continue using Korotkoff IV) the SOGAP panel advocate the use of mercury sphygmomanometers where available.

Assessment of Proteinuria

The distinction between *gestational hypertension* and *pre-eclampsia* is dependent on the diagnosis of "proteinuria". Within the ISSHP classification, the diagnosis of proteinuria may be made on the basis of either a 24 hour collection of urine (total protein excretion $\geq$ 300mg/24 hours) or reagent strip testing of two "clean-catch" urine specimens at least 4 hours apart ($\geq$ ++ protein; or $\geq$ + if urine specific gravity < 1.030 and pH < 8)[12].

Two recent studies[19,20] have highlighted the poor sensitivity and specificity of urinary dipstick testing for protein. The earlier study, by Kuo *et al*[19], suggested that dipstick values of "++" or greater could reasonably be accepted as abnormal in a clinical setting but that "+" and "trace" results are difficult to interpret. Unfortunately, the later paper, from Meyer *et al*[20], suggested that even dipstick values of "++" or more were associated with a false positive rate of over 10%.

Despite these research findings, the SOGAP group acknowledge that urinary protein estimation by dipstick testing is the only feasible method for use in a routine ante-natal clinic setting. The use of "++" as the cut-off for diagnosing *proteinuria* (as advocated by Davey and MacGillivray) should avoid most false +ves and the inclusion of a lower cut-off ("+") for women with dilute (SG < 1.030) and relatively acidic (pH < 8.0) urine should reduce the rate of false -ves. (Alkalinity of the urine increases the false +ve rate, therefore no compensation should be made for women whose urine is dilute but alkaline[12]). The negative predictive value of "-ve" or "trace" dipstick testing has been shown to be very poor (34%)[20], at least in hypertensive women. The negative predictive value in normotensive women is unknown and dipstick testing continues to be the only realistic clinic screening test.

In clinical practice, a dipstick reading of "++" may be regarded as diagnostic for proteinuria. A reading of "+" should prompt a check of urinary SG and pH and should only be regarded as diagnostic for proteinuria if SG <1.03 and pH <8.

2.2 PREVENTION OF GESTATIONAL HYPERTENSION

Recommendations

- Low dose aspirin in pregnancy results in only a very small reduction in the incidence of pre-eclampsia. Its use is not currently recommended for the majority of pregnant women. (**GRADE A**)
- Although evidence that calcium supplementation may be effective in preventing pre-eclampsia is accumulating, its use in routine practice is not yet recommended. (**GRADE C**)
- Other dietary interventions (eg vitamin, magnesium and zinc supplementation or sodium restriction) and pharmacological agents (eg PG precursors such as fish oils) cannot currently be recommended for the prevention of gestational hypertension and pre-eclampsia. (**GRADE A**)

Numerous dietary and pharmacological interventions have been suggested and investigated for the prevention of gestational hypertension and its sequelae. These interventions have recently been reviewed by Baker[21] and Dekker[22]. Calcium supplementation and low dose aspirin are the only interventions for which there is sufficient evidence to warrant consideration for routine clinical use.

Low Dose Aspirin

Collins (May 1994) has contributed a meta-analysis on "Antiplatelet agents for IUGR and pre-eclampsia" to the CPCD[24]. This meta-analysis incorporates results from the large Collaborative Low Dose Aspirin Study in Pregnancy (CLASP) and suggests that antiplatelet therapy (eg low dose aspirin) would reduce the incidence of pre-eclampsia by only a sixth. On this basis, the author calculated that 100 women would require to be treated to prevent one case of proteinuric pre-eclampsia. The conclusion from the meta-analysis is that available data "d*o not support the widespread, routine prophylactic use of antiplatelet therapy in pregnancy among all women judged to be at risk of pre-eclampsia or IUGR*".

Calcium Supplementation

A very recent meta-analysis by Bucher et al[23] has examined 14 RCTs (involving 2459 women) relating to the use of calcium supplementation. These authors conclude that calcium

supplementation is associated with an odds ratio for pre-eclampsia of 0.38 (95% CI, 0.22 - 0.65) and suggest that current evidence supports a policy of offering calcium supplementation to all pregnant women "in whom there is concern about the development of pre-eclampsia". (This might be interpreted as "all primigravidae".) The studies included in the meta-analysis have employed a wide range of regimens. A suitable regimen would comprise Calcium Gluconate 1g daily from 20 weeks gestation until delivery. Assuming an incidence of 10% among primigravidae, only 14 women would need to be treated to prevent one case of pre-eclampsia[23].

The SOGAP group gave careful consideration to the content of Bucher *et al*'s meta-analysis. The group shared the final conclusion of the authors that "*many more patient events are needed to confirm calcium's impact on maternal and fetal morbidity*", and were of the view that the strength and consistency of evidence in support of calcium supplementation is not yet sufficient to justify its introduction into routine care. Clinicians may, however, wish to consider calcium supplementation in women at particularly high risk of pre-eclampsia.

Dietary interventions

Baker[21] has reviewed available evidence on numerous dietary interventions for the prevention of pre-eclampsia. These include calorie restriction, salt restriction and supplementation, magnesium supplementation, zinc supplementation, manipulation of protein intake, supplementation of vitamins, particularly E, and N-3 fatty acid supplementation. Baker concluded: "*with very few exceptions, the better designed studies have failed to show any effect of dietary supplementation or restriction*" and "*until the appropriate research is performed in a less haphazard fashion, with all interventions performed in the context of controlled trials, no dietary intervention can be advocated*".

2.3 HYPERTENSION DETECTED AT BOOKING VISIT

Recommendations

- Hypertension detected for the first time at <20 weeks gestation may (rarely) be due to early onset gestational hypertension in the presence of molar pregnancy. Molar pregnancy should be excluded by ultrasound/biochemical assessment.
  (**GRADE B**)

- Women in whom hypertension is detected for the first time in pregnancy before 20 weeks gestation (after exclusion of molar pregnancy) should be investigated (to differentiate between primary, and secondary hypertension) and managed by a specialist with appropriate expertise.
  (**GRADE C**)

- Women known to have pre-existing chronic hypertension or renal disease should be managed during pregnancy by an obstetrician with access to a specialist physician.
  (**GRADE C**)

Gestational hypertension characteristically arises after mid-pregnancy except in the rare circumstance of molar pregnancy when an early onset condition with the characteristic clinical and microscopic features of pre-eclampsia can occur.

Although mild essential hypertension alone is generally associated with a good outcome for mother and baby (a reduced perinatal mortality rate associated with essential hypertension has been described by several authors[25,26]), it is associated with an increased incidence of pre-eclampsia and its consequent risks. Thus, the SOGAP group advocate that all women with known chronic hypertension be managed by a specialist obstetrician with access to advice from an interested physician although most will have good materno-fetal outcomes.

When previously undiagnosed hypertension is detected before mid-pregnancy, women must be appropriately investigated to exclude causes of secondary hypertension (eg phaochromocytoma, Cushing's syndrome). The US Consensus Report[8] emphasises that young, pregnant women are among the population in whom secondary hypertension is more apt to be found. Investigation and further management of such women should, again, be the responsibility of a specialist with appropriate expertise.

2.4 FACTORS INFLUENCING MANAGEMENT

Recommendations

- Women with unclassifiable hypertension (because pre-/early pregnancy BP recordings are unavailable) should be managed as having gestational hypertension .
  (**GRADE C**)

- Women meeting the criteria for gestational hypertension in whom an increase in diastolic BP of ≥ 25mmHg has occurred during pregnancy are at increased risk of poor fetal outcome and warrant enhanced surveillance.
  (**GRADE B**)

- Gestational hypertension arising at gestations of ≥ 37 weeks is often physiological but does warrant a programme of basic surveillance.
  (**GRADE B**)

The practice recommendations within this guideline apply to women with mild, gestational hypertension. The management of women with **severe** hypertension (as defined in the ISSHP classification) or with proteinuria is outwith the scope of the guideline. Similarly, as discussed above, the management of women with known chronic hypertension or with hypertension arising before mid-pregnancy should be by specialist teams and is outwith this guideline's remit.

Unclassifiable hypertension

The subgroup of women in whom hypertension first detected after mid-pregnancy is "unclassifiable" (because pre-pregnancy or early pregnancy recordings are unavailable), should be managed as having gestational hypertension according to the recommendations within this guideline. If such hypertension does not resolve in the puerperium, it must of course be investigated to exclude secondary hypertension .

Diastolic BP Increment

It has been suggested that women with gestational hypertension comprise two distinct groups. The first group represents "latent essential hypertension" and shares the feature of good fetal outcome enjoyed by women with mild essential hypertension. The second group represents "pre-proteinuric pre-eclampsia" and shares the feature of increased perinatal mortality suffered by women with true pre-eclampsia.

Redman and Jefferies[27] and, more recently, Perry and Beevers[28] have provided data suggesting that these two groups of women can be distinguished on the basis of the increment in diastolic pressure occurring during pregnancy. An increment of <25mmHg is, reportedly, associated with a favourable outcome, and an increment of ≥25mmHg is associated with a poor outcome.

Redman and Jefferies devised their "diastolic BP increment" criterion by analysis of a dataset relating to 16,211 pregnancies and tested its validity by application to a second dataset relating to 15,624 pregnancies. Perry and Beevers then tested the criterion in a prospective series of 692 pregnancies (of which only 55 met the criteria for gestational hypertension) and concluded that its use did select out a group of women sharing the poor outcome features of women with pre-eclampsia.

The SOGAP group acknowledges that the evidence supporting the validity of the "diastolic BP increment" criterion is somewhat scant, but is of the view that women with a rise in diastolic pressure of ≥25mmHg in addition to an absolute level of ≥90mmHg warrant a programme of enhanced surveillance.

Gestation at onset of hypertension

It is well documented[2,29] that diastolic blood pressure falls in the first two trimesters of pregnancy and rises in the third trimester towards non-pregnant levels. Thus, with increasing gestation, an increasing proportion of pregnant women will have diastolic pressures of ≥90mmHg. (Friedman and Neff[2] suggest that, among white multiparae, at ≥37 weeks gestation at least 5% will have diastolic pressures above this level compared with only 1% at 28 weeks.)

Friedman and Neff[2] have presented data on perinatal outcome in relation to blood pressure based on over 250,000 blood pressure recordings in almost 40,000 evaluable women, and have demonstrated that "*high diastolic levels seen any time in the third trimester are associated with much fetal wastage*". They show that diastolic pressures of ≥85mmHg recorded in the pregnancy "epochs" 37 to 38 weeks and 39 to 41 weeks are associated with fetal death rates of almost double those found with lower diastolic pressures.

Thus, although diastolic hypertension is increasingly common as pregnancy advances, and although perinatal death rates are low among infants delivered close to term, diastolic hypertension is nevertheless associated with an increased death rate and warrants a basic surveillance programme.

2.5 ASSESSMENT AND SURVEILLANCE

Recommendations
(GRADE C)

- Four levels of patient care are proposed in relation to the management of hypertension in pregnancy: **routine ante-natal care, basic surveillance, enhanced surveillance** and **specialist care** (outwith the scope of this guideline). Women may progress to and fro among these levels of care depending on changing clinical features.
- Women in whom hypertension is detected during routine ante-natal care should first undergo **preliminary assessment** to ascertain that the hypertension is not merely spurious. Where possible, this assessment period may best take place in the woman's own home.
- Hypertension is **not** confirmed during **preliminary assessment** unless it is observed to be sustained over a period of at least 4 hours.
- Those women in whom mild gestational hypertension is confirmed during preliminary assessment and whose diastolic BP does not exceed 100 mmHg should enter a programme of **basic surveillance**.
- Women in whom a diastolic BP ≥100mmHg is sustained, in whom the overall increment in diastolic BP is ≥25mmHg or in whom basic surveillance suggests poor fetal or maternal well-being should enter a programme of **enhanced surveillance**.

The cornerstone of management of women with gestational hypertension is assessment and surveillance rather than any form of active therapy. The aim of **assessment is** to exclude those women in whom hypertension in the ante-natal clinic setting is merely spurious (ie "white coat hypertension", or similar) from further intervention. The aim of **surveillance** is to monitor the progression of gestational hypertension and of maternal and fetal well-being.

Preliminary Assessment

The ISSHP definition of *hypertension* requires that a diastolic BP of ≥90mmHg be recorded on two or more consecutive occasions **at least four hours apart**. (While allowing that if the diastolic BP is ≥110mmHg, then the label of *hypertension* may be attached on the basis of a single recording). Davey and MacGillivray[12] acknowledge that "*the number of readings required to justify a diagnosis of hypertension is unknown*", but express the view that the "four hour" requirement accords with clinical experience and practice. The WHO Study Group[9] similarly base the diagnosis of *hypertension* on two readings at least four hours apart whereas the ACOG classification requires a six hour interval[13]. The SOGAP group acknowledge that the requirements of the ISSHP definition of *hypertension* have been devised on a purely empirical basis but support the concept that the diagnostic label should not be attached unless hypertension is observed to have been sustained over at least four hours. Women whose "spot" elevated diastolic is observed to return to normal in a period of less than four hours need not, of course, be detained for protracted observation and should be returned to routine ante-natal care.

The assessment period of ≥ 4 hours, when required, may take place in the hospital daycare facility, in the domiciliary setting (eg by means of repeat visits of the community midwife) or in a community setting by repeat attendance at the GP surgery. Assessment in the woman's own home may be optimal when it proves feasible.

Table IV Blood tests recommended in surveillance programmes: normal values during pregnancy

The Table indicates those tests where results in late pregnancy are usually **lower** than non-pregnant values by ↓ and those tests where results in late pregnancy are usually **higher** than non-pregnant values by ↑. Mean values (taken from: *Ramsay M. appendix of normal values in: James DK, Steer PJ, Weiner CP,, Gonik B. High Risk Pregnancy Management Options (1995) Pub. WB Saunders, London*) are provided for guidance. Management decisions based on laboratory results should be made in the light of local laboratories' reference ranges with allowance made for physiological changes in pregnancy as indicated.

TEST	EFFECT OF PREGNANCY	NORMAL VALUES
Haematological		
↓ platelet count	Falls, perhaps due to reduced lifespan.	Mean 260 x 10^9 /l at ≥36 wks
↑ platelet volume	Rises, due to increased number of 'young' platelets.	Mean 8.0fl at ≥36 wks
Renal function		
Electrolytes	Sodium, potassium chloride are almost unchanged.	As for laboratory references ranges
↓ Urea	Below non-pregnant levels throughout.	Mean 18.9mg/100ml at 36 wks
↑ Urate	Reduced during first trimester but above non-pregnant levels in late pregnancy.	Mean 232µmol/l at 36 wks Mean 269µmol/l at 38 wks
Liver function		
↑ Alkaline phosphatase	Late pregnancy values approx. double non-pregnant (due to placental & bone iso-enzymes). Levels do **not** reflect liver function reliably	Mean non-pregnant 61.6IU/l Mean 36 wks 139IU/l
γGT, AST, ALT) Bilirubin)	Unchanged.	As for laboratory reference ranges

The concept of initial assessment followed by graded levels of surveillance suggested by the SOGAP group is similar to the framework of management outlined in the US Consensus Report[8]. The investigations chosen for the assessment of disease progression and maternal well-being reflect the organ systems principally involved in the multi-system disorder of "gestational hypertension". Plasma urate is well documented as an indicator of fetal prognosis[30] as are measures of platelet consumption (including platelet volume)[31]. Similarly, liver function tests are advocated by the WHO Study Group[9] as being among the basic laboratory tests which reflect the progression of gestational hypertension.

Basic Surveillance

For those women in whom gestational hypertension is confirmed during the assessment period, a **basic surveillance** programme is the next step in management. The components of this programme, as suggested by the SOGAP group, are outlined in Fig. 2 and comprise: a single estimation of serum levels of urate, urea and electrolytes and full blood count including platelets; blood pressure recording and urine dipsticks testing twice weekly; a clinical appraisal of fetal size and well-being (ie abdominal palpation, fundal height measurement and enquiry into fetal movements), and clinical enquiry into maternal well-being. Acceptable ranges for basic surveillance blood test results are summarised in Table IV

Enhanced Surveillance

The SOGAP group are of the view that the programme of surveillance outlined above is sufficient for most women with mild gestational hypertension. However, those with a diastolic pressure sustained at >100mmHg, those where the overall increment in diastolic pressure is ≥25mmHg, and those where any abnormalities are suspected on the basis of the clinical and laboratory assessments undertaken during basic surveillance warrant a more intensive programme of enhanced surveillance. The only exception to this general guidance relates to women in whom gestational hypertension first presents at ≥ 37 weeks of pregnancy. Elevated diastolic BP, even if associated with an increment of ≥25mmHg, is often physiological in such women and, although it is associated with a modest increase in an already low perinatal mortality rate, is not felt to warrant more than basic surveillance.

The components of the enhanced surveillance programme, as suggested by the SOGAP group, are outlined in Fig. 2 and comprise: BP recording and urine dipsticks testing at least three times weekly; weekly serum estimations of those parameters included in *basic surveillance*, but with the addition of liver function tests; scan assessment of fetal growth and liquor volume and assessment by cardiotocography (or other means, eg Doppler ultrasound, as favoured locally) of fetal well-being. Clinical enquiry into maternal well-being should, of course, continue.

Specialist Care

As outlined previously, any woman with known chronic hypertension or renal disease, any woman developing **severe** hypertension (diastolic BP sustained at 110mmHg) or proteinuria (≥ "++" on dipstick testing, or ≥ "+" for women with urine SG < 1.030 and pH <8) and any woman who develops features of fetal or maternal compromise during **enhanced surveillance** should be referred to her consultant obstetrician for appropriate assessment and further management (which may well include assessment for delivery) which is outwith the scope of this guideline.

FIGURE 2 LEVELS OF CARE FOR WOMEN WITH GESTATIONAL HYPERTENSION

LEVEL OF CARE	RELEVANT WOMEN	COMPONENTS OF CARE PROGRAMME
ROUTINE ANTENATAL CARE	• Normotensive women • 'Spot' hypertension not sustained on assessment	
ASSESSMENT	• 'Spot' hypertension recorded during routine antenatal care	• BP recording on >=2 occasions >=4 hrs apart
BASIC SURVEILLANCE	• Hypertension confirmed on assessment • Any mild hypertension arising at >37 weeks	• BP recording twice weekly • Urine 'dipstix' twice weekly • Clinical appraisal fetal size/well-being • Enquiry *re* maternal well-being • Single estimate serum urate U&Es, FBC, platelets
ENHANCED SURVEILLANCE	• Diastolic sustained at >100mmHg • Diastolic increment >25mmHg • Clinical suspicion IUGR • Clinical suspicion poor maternal/fetal well-being • Abnormal results on basic surveillance blood tests	• BP recording at least 3 times per week • Urine 'dipstix' at least 3 times per week • Weekly serum urate, U&Es, FBC, platelets, LFTs • Scan assessment fetal size & liquor vol • CTG (or other) assessment fetal well-being
SPECIALIST MANAGEMENT (OUTWITH GUIDELINE)	• Severe hypertension • Proteinuria • Abnormal findings during enhanced surveillance	OUTWITH THIS GUIDELINE

CLINICAL ILLUSTRATIONS OF USE OF GUIDELINE RECOMMENDATIONS

◊ **Miss AB,** a 19 year old primigravida, attends her community midwife at 30 weeks gestation for routine ante-natal care. Her blood pressure is found to be elevated at 130/92. Urine dipstick testing reveals no proteinuria. Miss AB is left quietly seated for 20 minutes and her BP rechecked. The recording is now 132/90.

➔ Miss AB requires **assessment** over a period of at least four hours before the diagnosis of *hypertension* is confirmed. She is allowed to return home and arrangements made for the midwife to visit her at home the same evening. When the midwife checks her BP at home (five hours later) it measures 125/85. The diagnosis of *hypertension* is not confirmed and Miss AB is returned to the schedule of routine ante-natal care.

◊ **Mrs CD,** a 35 year old primigravida, attends her hospital ante-natal clinic for a routine visit at 34 weeks gestation. Her diastolic BP measures 95 and 92mmHg on two occasions ten minutes apart in the clinic. She is transferred to the hospital day care facility for **assessment** and her diastolic BP is found to be sustained at 90mmHg over a period of four hours. A diagnosis of gestational hypertension is made and Mrs CD enters the **basic surveillance** programme.

➔ Dipstick testing reveals no urinary protein, blood is taken for basic investigations. The uterine fundus is found to measure only 30cm from the pubic symphysis.

➔ Thus, the clinical assessment of fetal size undertaken within **basic surveillance** raises the suspicion of IUGR and Mrs CD becomes a candidate for the **enhanced surveillance** programme. She is referred for scan assessment of fetal size and CTG assessment of fetal well-being.

◊ **Mrs EF**, a 23 year old primigravida, attends her hospital ante-natal clinic for a routine visit at 34 weeks gestation. A diastolic BP of 93mmHg is recorded in the clinic and confirmed to be sustained over a period of 4 hours during observation in the day-care ward. Dipstick testing of urine reveals "+" proteinuria with an SG of 1.04 and pH 8.3.

➔ The requirements for the diagnosis of proteinuria based on dipstick testing have not been met. Mrs EF should be regarded as having mild, non-proteinuric hypertension and managed according to the basic surveillance programme.

◊ **Mrs GH**, a 25 year old primigravida, attends her community midwife at 36 weeks gestation for routine antenatal care. Her blood pressure is found to be elevated at 140/95. Urinalysis is negative, the fundal height measures 37cms and fetal movements are frequent. **Assessment** is arranged in the form of a home visit by the midwife later that day (after an interval of >4 hours). At this visit, Mrs GH's blood pressure again measures 140/95

➔ Mrs GH becomes a candidate for **basic surveillance**. The midwife arranges for her to attend the surgery again the following day for blood to be taken and for repeat blood pressure recording and urinalysis. Thereafter, arrangements are made for the midwife to visit Mrs GH at home twice weekly until signs either resolve or progress.

2.6 TREATMENT

Recommendations

- Hospitalisation and bed rest are of unproven value in the management of mild, non-proteinuric gestational hypertension.
  (**Grade A**)
- Anti-hypertensive drug treatment is not usually indicated for women with non-proteinuric gestational hypertension. Where diastolic BP > 100mmHg or where the disease has arisen at < 32 weeks gestation consideration may be given to antihypertensive therapy.
  (**Grade A**)
- When anti-hypertensive drugs are used, methyldopa may be considered as the most appropriate first-line agent although other drugs, eg labetalol, which may be preferred by some clinicians are acceptable alternatives.
  (**GRADE B**)
- Although delivery is the definitive treatment for gestational hypertension, mild, non-proteinuric disease does not, in itself, constitute an indication for induction of labour.
  (**Grade C**)

Duley (1993) has contributed a meta-analysis on "*Hospitalisation for non-proteinuric pregnancy hypertension*" to the CPCD[32]. This meta-analysis included only three trials examining the value of bed rest in hospital on feto-maternal outcome. No significant differences between hospitalised and non-hospitalised women were found in relation to any of the outcomes studied, but confidence intervals were wide and available data were regarded as inadequate.

Duley (1994) has provided a further meta-analysis on "*Any anti-hypertensive therapy for pregnancy hypertension*"[33]. This overview incorporates results from 23 trials in women with "mild" or "moderate" pregnancy hypertension. Overall, treatment significantly reduced the risk of developing severe hypertension or proteinuria and also the risk of respiratory distress syndrome (RDS) in the neonate. There were no significant differences in relation to any of the other outcomes studied, and the conclusion of the reviewer was that there are currently insufficient data on safety and efficacy to recommend routine clinical use.

One of the most recent, UK trials included in Duley's meta-analysis is that of Pickles et al[34,35] who conducted a randomised trial of labetalol vs. placebo in women with "mild to moderate pregnancy induced hypertension (PIH)" (diastolic 90 - 105mmHg). This trial examined both neonatal (birthweight) and maternal (in-patient days, proteinuric pre-eclampsia and perceived need for induction) outcomes. The results of this study were in accord with those of Duley's meta-analysis in that the treated group experienced significant falls in BP and were significantly less likely to develop proteinuria. However, gestational age at delivery, onset of labour and mode of delivery were unaffected suggesting that obstetric intervention (perceived need for early delivery) was uninfluenced by pharmacological treatment. These authors concluded: "*our results add to the growing consensus that while mild to moderate PIH must be carefully monitored, pharmacological treatment of the disease does not materially influence outcome*". They concede however, that for disease presenting before 32 weeks gestation, the reduction in the development of proteinuria associated with anti-hypertensive therapy may be advantageous.

Thus, the SOGAP Group regard the recommendation that anti-hypertensive medication should not be used for gestational hypertension (at least for diastolic pressures of < 100mmHg and for disease onset at > 32 weeks) as being a reasonable interpretation of research evidence available to date.

It is emphasised in the US Consensus Report[8] that '***Both maternal and fetal assessment must be carried out meticulously regardless of the degree of blood pressure control***' in

recognition of the fact that pharmacological BP reduction is only influencing the clinical sign of gestational hypertension **not** the underlying disease process which places the fetus at risk.

The US Consensus Report[9] includes a lengthy discussion on the relative merits of different drugs for the reduction of BP in pregnancy. This document emphasises that choice of drug in these circumstances should be governed by information on '*efficacy to reduce blood pressure and also on the acute and long-range effects on fetal well-being especially long-range neurological effects*.' and states: '*So far, only one drug, methyldopa, meets these criteria. Thus, if feasible, methyldopa therapy should be chosen in pregnancy*'. Methyldopa does at least have the advantage of 10 year follow-up data on children exposed in utero[36].

Thus the SOGAP Group recommend that in those few cases of gestational hypertension where anti-hypertensives are indicated, the centrally-acting adrenergic inhibitor methyldopa is the first-line agent of choice but where side-effects or physician-unfamiliarity dictate otherwise, the α/β blocking agent, labetalol, may be a suitable alternative. Concerns were expressed by SOGAP group members regarding labetalol's negative inotropic effect on the mother and adverse effects on the fetus, including impaired glycaemic control and altered pulse rate.

2.7 PLACE OF MANAGEMENT

Recommendation

- Monitoring and management of non-proteinuric gestational hypertension is often best undertaken (in terms of both clinical- and cost-effectiveness) on a day-care or community basis. (**GRADE B**)

Non-proteinuric pregnancy hypertension can be monitored and managed in at least three different settings: hospital in-patient, hospital day-care and domiciliary. Several studies have compared these management settings in terms of both clinical- and cost-effectiveness. Duley (1993) has contributed a meta-analysis on "*Hospitalisation for non-proteinuric pregnancy hypertension*" to the Cochrane Pregnancy and Childbirth Database (CPCD)[32] which included only three studies, but showed no significant differences between hospitalised and control patients with respect to any of the outcomes studied (including development of severe or proteinuric disease pre-term delivery, low birthweight and perinatal death).

Twaddle and Harper[37] have undertaken an economic appraisal relating to day-care (as opposed to in-patient care with prior domiciliary visits) and concluded that, for most women with non-proteinuric pregnancy hypertension, day-care is the most cost-effective management setting.

The SOGAP Group acknowledge that geographical factors influence the most appropriate setting for the management of non-proteinuric pregnancy hypertension for individual women. The Group consider that the ASSESSMENT and SURVEILLANCE 'packages' outlined in this Guideline can appropriately be delivered in a variety of settings: domiciliary, day-care or in-patient. A fundemental aim of the recommendations within this guideline is to reduce unnecessary hospital admissions among women with mild gestational hypertension. The community-based team of General Practitioner, Community Midwife and their support staff are able, in many instances, to undertake monitoring and management of such women.

It is suggested that protocol groups adapting this Guideline for local use might address the issue of the most appropriate management setting to meet the needs of their own patient group.

2.8 MANAGEMENT AFTER DELIVERY

Recommendations

- Women who have experienced non-proteinuric gestational hypertension are at increased risk of essential hypertension in later life and should be targeted for advice on life-style changes (eg reduced sodium intake, weight reduction, exercise) which may reduce this risk.
  (**GRADE B**)

- The blood pressure of women who have had gestational hypertension should be checked at 6 weeks post-delivery. If BP has not returned to normal levels, appropriate investigations to exclude secondary hypertension should be initiated.
  (**GRADE C**)

It is well documented that true pre-eclampsia is an intrinsic, pregnancy-related event unrelated to future risk of essential hypertension. Non-proteinuric gestational hypertension however, does represent "latent essential hypertension" in a proportion of women and is associated with an increased risk in later life[38]. It seems appropriate therefore to target such women for lifestyle measures such as those advocated in the Report of the US Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure (JNCV)[39].

Post-delivery care of all women with hypertension in pregnancy must, of course, include BP recording at the traditional six-week post-natal check and appropriate further investigation and management of any women in whom BP has not returned to normal.

Statement of Intent

This guideline is not intended to be construed or to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns evolve.

These parameters of practice should be considered recommendations only. Adherence to them will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor in light of the clinical data presented by the patient and the diagnostic and treatment options available.

Significant departures from the local protocol should be fully documented in the patient's case notes at the time the relevant decision is taken.

A background paper on the legal implications of guidelines, prepared by Dr Pamela Abernethy of Simpson and Marwick W.S., is available from the SIGN secretariat.

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APPENDIX I

SUGGESTED MINIMUM DATA SET FOR AUDIT OF THE CARE OF WOMEN WITH MILD, NON-PROTEINURIC HYPERTENSION IN PREGNANCY

Applicable patients: All women delivering a live or stillborn baby who had a diastolic BP of ≥90mmHg recorded antenatally on one or more occasions.

1	Unique identifier, eg hospital number		
2	Did diastolic BP exceed 110mmHg at any time?	No/Yes; if Yes, STOP	
3	Was ≥ '++' proteinuria detected on dipstix testing at any time?	No/Yes; if Yes, STOP	
4	What was the maximum diastolic BP recorded antenatally?	.....mmHg	
5	Increment between minimum and maximum diastolic BP recorded antenatally	.....mmHg	
6	No. of weeks gestation at which a diastolic BP of ≥90mmHg was **first** recorded	.....weeks	
7	Was patient admitted to hospital antenatally?	No/Yes	
8	If yes, was assessment of hypertension the **principal** reason for admission?	No/Yes/Not assesaable	
9	If Yes, no. of **nights** spent in hospital for antenatal assessment		
10	Was labour induced?	No/Yes	
11	If yes, was hypertension the **principal** reason for induction?	No/Yes/Not assessable	
12	Tests undertaken antenatally:	Tick if undertaken	No. of times done
	I) serum urate		
	ii) urea and electrolytes		
	iii) FBC		
	iv) platelet count		
	v) liver function tests		
	vi) ultrasound scan at >24 weeks		
	vii) doppler ultrasound		
	viii) antenatal CTG		
	ix) 24 hour urine collection for protein estimation		