ESSENTIAL HYPERTENSION IN PREGNANCY

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A DIFFICULT task confronts the obstetrician who attempts to define and to elucidate the incidence of essential hypertension in pregnancy, because the highest levels of the normal arterial blood-pressure in pregnant women have not yet been determined. Blood-pressure readings are a relative innovation in the obstetric world and it is to our colleagues the physicians we must turn for information as to the upper limits of normal blood pressure in women of child-bearing age. The guidance we receive from them is, unfortunately, neither clear nor unanimous, for small rises that are important to the obstetrician appear trivial to the physician. Perhaps the figures due to Masters, Dublin and Marks (1950) are the most accurate:—

Age 20 to 29—Range	100–130	mm. Hg
	60–86	
Age 30 to 39—Range	105–140	mm. Hg (a particular rise occurring after the age of 37)
	60–90	

It makes matters very complicated, however, for hypertension to be diagnosed above different levels in pregnant women of different ages, so for convenience of discussion and assessment of results it would be advisable to agree upon an upper limit of normal blood pressure for pregnant women of all ages. When this figure has been determined we can then define essential hypertension in pregnancy as a condition in which it is exceeded in the absence of any known cause.

Pickering (1955) considers that any dividing line between a normal and a high blood pressure is artificial and that hypertensive patients are merely the tail end of a skewed Gaussian curve of distribution. However, Platt (1959), from a study of bimodal blood-pressure curves obtained from the siblings of middle-aged hypertensive patients, believes that essential hypertension is a specific entity, possibly due to an inherited dominant Mendelian gene. Whichever view is correct the fact remains that the pregnant hypertensive patient requires especial care, and it is important, therefore, to have a standard whereby the disease may be diagnosed so that the appropriate treatment may be given to her.

F. J. Browne (1935), who must be considered a pioneer in this field, first suggested 130/70 mm. as being the upper limit of normal blood-pressure in women of child-bearing age, but later changed these figures to 120/80. Most observers consider these limits to be rather low, an attitude which is forced upon them by the shortage of ante-natal beds. With obstetricians being guided by their individual experience to select their own levels at which hypertension may be diagnosed, the author chose the figure of 130/80 mm. Hg. It was found, however, that when the booking blood-pressures were taken during the first 20 weeks of pregnancy, only 69% of patients had a normal pressure; 18% had either the systolic or diastolic pressure raised, whilst in 13% both figures were exceeded. If 130/80 is taken as the upper level of normal, therefore, it indicates that 31% of patients are hypertensive. As results based on such a large proportion of patients would give a misleadingly favourable prognosis with an abnormally low incidence of complications, a higher standard should probably be taken. The selection of a standard in this arbitrary manner explains the diversity of different investigators' results, who not only employ their own standards, but sometimes do not even state what they are. Vartan (1958) has compared the standards employed by 10 different hospitals and concludes that we are in a 'chaotic state'.

In addition to this fundamental indecision, obstetricians are not agreed whether the diagnosis should be based on the initial blood-pressure taken when the patient first attends the ante-natal clinic (the casual pressure), or on the pressure obtained after some hours of mental and physical rest (the basal pressure). There is agreement that it should be taken during the first 20 weeks of pregnancy so that confusion does not arise with the raised pressure of pre-eclampsia, and that it should also exclude raised pressures secondary to acute and chronic nephritis, chronic pyelonephritis, polycystic kidney, pheochromocytoma, Cushing's disease, and coarctation of the aorta, but there is no uniformity of opinion whether a single raised reading constitutes the diagnosis or whether it should be repeated or sustained.

To add to these difficulties, there is one which is equally great. This is the difficulty of estimating the correct blood-pressure of the patient. It is true that nervousness, excitement, and exercise may influence the readings, but in addition, we have to consider the effects of the attitude of the patient, the height of the sphygmomanometer in relation to the heart, the size of the arm-band (which should be 30×13 cm.), the circumference of the arm, the calibration of the instrument, the accuracy of the zero, the uprightness of the scale, the effect of parallax, the sharpness of the meniscus, and its free communication with the atmosphere. All these factors should be allowed for in taking pressure readings but in particular a correction factor should be applied for the fatness or thinness of the arm, as this may cause variations amounting to 40 mm. in the systolic pressure and 25 mm. in the diastolic. During the reading there is agreement that the point at which the sound appears with the fall of the mercury corresponds to the systolic pressure, but there is still discussion, and pleas for uniformity, upon the point which indicates the diastolic pressure. Most observers take this as the level at which the quality of the sounds alters, although there are many, including most American writers, who prefer the point at which the sounds completely disappear. Lack of agreement in this matter adds further to the difficulty of interpreting different workers' results, a fact which must be duly noted when considering the figures quoted later.

Pathology

The raised blood-pressure of essential hypertension is maintained by a state of arteriolar spasm mediated through the vaso-motor centre and the peripheral autonomic ganglia. In its early stages it is essentially a functional disorder and there is no morbid anatomical basis. The precise mechanism of its aetiology has not yet been determined, but genetic, neurogenic, dietetic, renal, and endocrine factors have all been implicated. At present a neurogenic basis holds the field, based on a study of the blood-pressures of animals exposed to stressful situations, but this cannot be accepted unreservedly as there is no evidence of increased autonomic activity shown by raised catechol amine production in essential hypertensive cases as there is in patients with pheochromocytoma. When sympathetic influences are removed there still remains some arteriolar tone, due perhaps to hormonal or electrolytic factors, and these, particularly in pregnancy, may well play a role in the pathogenesis of this disease. Thus Duff (1958) has described an increased arteriolar spasm induced by adrenaline after the administration of hydrocortisone, and he

considers the suprarenal cortex may be involved in its aetiology.

At a later stage secondary effects follow, and there ensues, particularly in the kidney, a medial degeneration with a compensatory intimal proliferation in the arteriolar wall. In malignant cases, where the blood-pressure is extremely high with a diastolic pressure exceeding 130 mm., a fibrinoid arteriolar necrosis occurs which heralds the rapid deterioration seen in this condition. This phase may occur secondary to nephritis or pyelonephritis, but in any event is rarely encountered during pregnancy.

Clinical Course of Pregnancy

Usually there are no symptoms referable to the hypertensive state and the diagnosis rests purely upon the level of the blood-pressure. There may be cardiac enlargement in long-standing cases, and the typical changes of hypertensive retinopathy may be seen in the silver-wiring of the retinal arteries and the obstruction to the retinal veins. In normal pregnancy the blood-pressure falls during the second trimester, as was first shown by Hare and Karn in 1929. This may be due to the loss of tone of the smooth muscle throughout the body as a consequence of the increased production of progesterone. Duff (1958) considers it results from the increased output of oestrogens occurring at this time, whilst Burwell (1938) thinks it is due to the arterio-venous shunt effect of the placental circulation. The fall is similarly seen in cases of essential hypertension, as was first described by Reed and Teel (1938), when the high readings obtained in the first trimester become replaced by lower readings in the second trimester. In the final trimester, however, the blood-pressure may take different patterns:—

1. The readings may rise to the original levels obtained early in pregnancy, and the patient continues with her original degree of hypertension unchanged. There is then no oedema or albuminuria, and the blood-urea and renal function tests remain normal.

2. The blood-pressure may rise to heights considerably in excess of those of early pregnancy. In the absence of treatment readings in the region of 220/140 may be obtained, in which case the patient may complain of headache, and is in danger of cardiac and cerebral catastrophes. Oedema and albuminuria are still absent and estimation of the blood-urea and renal function tests give normal results in these cases.

3. Pre-eclamptic toxæmia may become added to the essential hypertension, and the patient develops oedema of face, hands and feet, increasing elevation of the hypertension, and in more serious cases, albuminuria. Again the patient is in

danger, on this occasion from developing eclampsia itself. Vartan (1958) however, has pointed out the rarity with which eclampsia supervenes in these cases, as only 5% of eclamptics start pregnancy with a diastolic pressure exceeding 90 mm. Possibly this is a testimony to their effective management.

4. Occasionally malignant hypertension may supervene, in which case there is rapid deterioration of the patient, with increasing blood-pressure, renal failure, rising blood-urea, marked retinal changes, and ultimately death.

During the second half of pregnancy the foetus is at risk. It has been shown by Browne and Veall (1953) that the placental circulation is reduced in hypertensive patients, and as is well known the hazards of infarction and retroplacental bleeding are then more likely to occur. If the patient exceeds her expected dates the placental circulation is still further reduced, and even in the absence of these major hazards, the outlook for the foetus then becomes poor.

Differential diagnosis

There may be a family history of hypertension, but this is rarely obtained in the antenatal clinic. Of paramount importance here is the level of the blood-pressure in early pregnancy. Whereas in a typical case of pre-eclampsia the blood-pressure is normal for the first two trimesters and then rises during the final three months, in essential hypertension it is raised in the early months, may fall slightly during the middle trimester, and then rises again in the final three months. If the patient is first seen towards the end of pregnancy with a raised blood-pressure and no additional signs, the differential diagnosis between essential hypertension and pre-eclampsia is made by referring to the blood-pressure levels of early pregnancy. In both conditions the blood-urea and renal function tests are normal.

In cases of chronic nephritis the same triad of physical signs may be present. Again the blood-pressure may be raised in early pregnancy and after a mid-pregnancy drop rise again in the final trimester. Oedema and albuminuria may in this event occur throughout pregnancy, whilst retinopathy, a high blood-urea, urinary casts and impaired renal function tests complete the picture.

Other renal lesions which may cause hypertension during pregnancy should be diagnosed without the aid of radiography at this time. Thus polycystic kidneys may be suspected by palpation of the enlarged kidney masses, and the patient will be found to pass abundant quantities of dilute urine, perhaps containing a trace of albumin, but free from casts and cells. In cases of chronic pyelonephritis evidence of infection will be present

in the urine, but repeated examinations may be necessary as the excretion of pus cells and bacteria tends to be intermittent. Coarctation of the aorta should be suspected if the femoral pulses cannot be palpated. Examination of the chest wall may then reveal the presence of pulsating collateral subcutaneous arteries, while radiography of the thoracic cage may show notching of the ribs. Marked difference of blood-pressures in the arms and legs may also be obtained. In cases of pheochromocytoma the patient characteristically complains of spasmodic attacks of headache, nausea or vomiting, sweating, palpitations, and pallor, separated by intervals of relatively normal health, and the hypertension will be found to be labile rather than sustained. The diagnosis is not difficult to make if the condition is borne in mind, and it may be confirmed by estimation of the catechol amines in the blood and urine. Cushing's disease is very rare in pregnancy, but may be suspected if the hypertension is associated with adiposity, hypertrichosis, hyperglycæmia, glycosuria, and excessive lineæ gravidarum.

Prognosis in relation to pregnancy *Infertility*

Johnson (1958) has pointed out that hypertensive patients tend to be infertile, as their first pregnancy occurs at an average of six years after marriage, compared to a period of two years in normotensive patients of the same age.

Incidence of Abortion

Morris (1958) did not find a high incidence of abortion amongst 490 patients who had a diastolic pressure of 90 mm. or more at or before the sixteenth week of gestation, as only three aborted spontaneously, whilst a further three threatened to do so but subsided.

Maternal prognosis with uncomplicated hypertension

Browne and Dodds (1942) found that in a series of 239 patients 17% passed through pregnancy with their hypertension unchanged, whilst 61% developed a rising blood-pressure as pregnancy progressed. Morris on the other hand has described quite different trends. He found that in 53.5% of 480 patients the raised blood-pressure was stable, in 18.8% it fell from its initial high level and remained low throughout pregnancy, in 11% it fell in mid-pregnancy and rose again to within 20 mm. of its original level, whilst in 8.8% it rose to higher levels in the final trimester. Morris comments on the rarity of the late rise in his patients, and emphasizes that in 71 pregnancies when the initial systolic pressure exceeded 160 mm. the final pressure rose above this figure on only four occasions. He found there was no

increased weight gain in the hypertensive patients compared to pregnant patients in general. All authors are agreed that maternal cerebral and vascular accidents are very rarely encountered as hypertensive complications today.

Accidental hæmorrhage

In a series of 673 hypertensive patients Browne (1958) found the incidence of accidental hæmorrhage to be 6.6% whilst Gate (1960) reported only one case (1.4%) among his 73 patients with a blood-pressure in excess of 150/100 mm. before the twentieth week of pregnancy. Morris reported accidental hæmorrhage to occur in 2.3% of his cases, all of whom had an initial systolic pressure below 160 mm., which was exceeded later by only one patient.

Fœtal prognosis

The hazard to the fœtus is very great because of the reduction in the maternal placental circulation. Contrary to expectations the proportion of small babies born to hypertensive mothers is not increased—at least not until the higher ranges of hypertension are reached. Thus Morris (1958) found the incidence of prematurity to be about 14% in patients with an initial systolic pressure below 160 mm., 22% with pressure between 160 and 179 mm., and 30.8% above 180 mm.

In Browne and Dodd's (1942) series, the fœtal and neonatal mortality rate was 16.2%, whilst Taylor, Tillman and Blanchard (1954) reported a fœtal loss of 15.7% in 372 cases. Browne (1958) had a fœtal and neonatal mortality rate of 7.9% despite a surgical induction rate of 41.2% and a Cæsarean section rate of 11.7% (which compared with overall rates of 11% and 5%).

If the blood-pressure early in pregnancy exceeds 150/100 the fœtal prognosis is worsened. Thus Browne (1958) reported a fœtal and perinatal loss of 68% in this event, but Gate's (1960) smaller series sustained a fœtal loss of only 8%. He ascribed this excellent result to mental and physical rest, hypotensive drug therapy, induction of labour (in 37% of cases), and Cæsarean section (21% of cases). Morris (1958) reported a loss of 6.7%, but pointed out that when the initial systolic pressure exceeded 160 mm. the loss amounted to 12.2%. Patients with a rising blood-pressure had a higher perinatal loss (12.8%) than those in whom the pressure level was constant (6.1%).

In cases where the initial systolic pressure exceeded 180 mm. Browne (1958) did not obtain a single living child, but Gate was able to rescue 12 live children from 15 such patients.

Townsend (1959) has emphasized the correlation existing between the perinatal mortality rate and the initial diastolic pressure of early pregnancy. He found that with an initial diastolic pressure between 90 and 99 mm., the associated fœtal loss was 4%, with an initial pressure between 100 and 109 the loss was 6%, and with a high initial pressure exceeding 110 mm.Hg, the loss amounted to 16%.

Johnson (1958) has shown that age has an important influence on the fœtal prognosis, as his overall perinatal death rate was 7.6% in patients under 35 years of age, and 24.3% in those who exceeded this age.

Superimposed pre-eclampsia

Browne and Dodds (1942) reported that 17.9% of their 239 patients developed pre-eclamptic toxæmia, Browne (1958) found it to occur in 35.5%, whilst Gate (1960) had an incidence of 57%. Morris (1958) found that pre-eclampsia (diagnosed by the presence of albuminuria, measurable on the Esbach scale) was superimposed in 5.5% of cases, but was present in 21.4% of cases where the initial systolic pressure exceeded 180 mm. He had one patient who developed eclampsia, her initial pressure being 135/90.0. He could not find any excessive weight gain associated with the appearance of pre-eclampsia. This observation has recently been confirmed by Matthews (1961).

Among hypertensive patients with superimposed pre-eclampsia Gate reported a fœtal loss of 9.5% and Morris one of 35.3%. Johnson (1958) emphasizes the importance of the time of superimposition of pre-eclampsia. He found that if this developed before the thirtieth week of pregnancy there was a perinatal loss of 71.4%, but when it occurred during the last month the loss was 9.6%; the severity of the pre-eclampsia also influenced the fœtal loss, for this amounted to 23% when it was marked (diastolic pressure over 110 mm. and albuminuria), and 14.3% when it was only moderate.

Townsend (1959) has shown that the appearance of albuminuria worsens the fœtal prognosis. Thus he found that patients with an initial diastolic pressure of 90 to 99 mm. had a fœtal loss of nil in the absence of albuminuria and of 14% when albumin was present; those with initial pressures ranging between 100 and 110 mm. had corresponding rates of nil and 50%, whilst those exceeding 110 mm. also had rates of nil and 50%. The appearance of albuminuria is so harmful to the fœtus that any method whereby this could be prevented would be of value. Apart from rest none is known at present. Townsend has, however, pointed out that if there is a mid-pregnancy drop

of 10 mm. in the diastolic pressure the chance of developing albuminuria is reduced, whilst with a drop of 20 mm. it is almost eliminated. If the diastolic pressure during the third trimester falls below its initial level, albuminuria rarely occurs.

Management

When first seen in the antenatal clinic during early pregnancy the patient with hypertension should be admitted to hospital for investigation and diagnosis. With rest in bed the basal level of the blood-pressure is determined, and patients with organic causes of hypertension referred to above may be diagnosed and treated. If no cause can be found the diagnosis of essential hypertension may be made, and the treatment then depends upon its degree. If it is below 150/90 the patient may be discharged from hospital, but she should be enjoined to live a quiet life during pregnancy and to secure a good night's sleep. She should be seen at weekly intervals in the ante-natal clinic or by her general practitioner and readmitted to hospital if there is any worsening of her condition.

If the blood-pressure reaches 150/90 when she is first seen, or if it rises to this figure later in pregnancy but before the fœtus is mature, she should be treated by hypotensive drugs. There are many of these drugs now available, of which guanethidine sulphate (Ismelin) can be recommended. This is not a ganglion-blocking agent, but instead selectively inhibits the peripheral sympathetic system. The patient should remain in hospital while the correct dosage is decided upon. Thus she may be given 10 mg. daily by mouth increasing by 10 mg. every four days until the optimum controlling dose is determined and she is stabilised with a pressure at normal levels on standing; the dosage can be guided simply by the response of the hypertension and there is no risk of paralytic ileus or constipation. The patient should then be discharged, subsequently to be seen weekly at the clinic, when the dosage may be altered or the patient readmitted as appears necessary. Sedation such as phenobarbitone $\frac{1}{2}$ gr. twice daily may also be given.

If the pressure rises persistently above 160/100 the patient should be kept in hospital and given complete rest in bed while the hypotensive therapy is continued. There are now additional hazards to be guarded against. Firstly steps must be taken to avoid foetal death if possible, by increasing the placental circulation. It was shown by Morris, Osborne and Payling Wright (1956) that the circulation through the uterine wall, which is already reduced by hypertension, is further reduced by exercise but is increased by

rest; accordingly complete immobilization in bed is advisable in these cases for the sake of the fœtus. Rest may also help in preventing the development of pre-eclampsia. Should œdema develop in these cases chlorothiazide may be given, 1 g. daily for three days every week, to augment diuresis and incidentally potentiate the effect of the hypotensive drug. Sedation, vitamins, essential minerals, and an hypnotic at night may be employed.

As there appears to be no excessive weight gain in hypertension patients, even in those in whom the supervention of pre-eclampsia is imminent, there appears to be nothing to be gained by instituting a regime of weight control by carbohydrate restriction. Many authorities, however, recommend a low sodium diet for these patients.

Should pre-eclampsia be superimposed on the hypertension and albumin appear in the urine the risk to the fœtus as already pointed out becomes greater, and immediate admission to hospital is necessary. The albuminuria may disappear after immobilisation in bed, sedation, diet control, and diuresis, but if it persists the pregnancy should be terminated as soon as the fœtus is considered of sufficient weight to be viable. This may be a difficult decision to reach, not only in estimating the foetal weight, but also in balancing the chances of death from prematurity during and after delivery against those from intra-uterine accidents if labour is too long deferred. When termination is decided upon, delivery should be effected by surgical induction or by Cæsarean section as the gravity of the case demands. This should also be done if the systolic pressure reaches 180 mm. for fear of the occurrence of cardio-vascular accidents, although these are unlikely to occur if hypotensive drugs are being used. Pregnancy should also be terminated at any time, even before foetal viability is reached, if changes due to malignant hypertension make their appearance. Vartan (1958) has pointed out that a falling blood-pressure and lessening of albuminuria, combined with a loss of weight, are bad prognostic signs for the fœtus, which should be delivered forthwith by section.

If the pressure remains under control without any added toxæmia there is no immediate need for termination, and the patient may then be allowed to continue under treatment until term. She should not, however, be permitted to exceed the expected date of delivery. This is because the placental circulation is reduced after term and if this reduction is added to that caused by the hypertension, the consequences to the fœtus may be serious. When the patient reaches term therefore, labour should be induced by medical or surgical means. Should she not respond to

Summary

1. Essential hypertension in pregnancy is defined.

2. Fallacies involved in the correct determination of the arterial blood-pressure are described.

3. The differential diagnosis of conditions giving rise to hypertension during pregnancy is outlined.

4. A review is given of the clinical course of pregnancy in hypertensive subjects, with the frequency and significance of incidental complications.

5. The management of pregnancy and labour in hypertensive patients is discussed.

6. The prognosis is described both during the immediate pregnancy and subsequently.

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