# CARDIAC OUTPUT IN HYPERTENSIVE TOXAEMIAS OF PREGNANCY

BY

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RIGHT heart catheterization, introduced by Cournand and Ranges (1941), has proved to be the most reliable method of determining cardiac output not only in health but also in disease. This method has been used by several workers to investigate the behaviour of the cardiac output in normal pregnancy (Werkö *et al.*, 1948; Palmer and Walker, 1949; Hamilton, 1949a). The results obtained by Palmer and Walker, and by Hamilton agree closely and show that the maximum increase in cardiac output is of the order of 27 per cent above the non-pregnant level and is attained during the 26th to 29th weeks of pregnancy. The output virtually returns to normal levels during the last 3 weeks of pregnancy.

When the study of the normal range of variation in cardiac output during pregnancy had been completed the investigation was extended to cases of toxaemia of pregnancy. All the toxaemic patients investigated shared the common feature of hypertension and the results of the first 44 cases of toxaemia were reported by Hamilton (1950). They showed that an increase in cardiac output was found in some cases of hypertension, some cases of pre-eclampsia and in all cases of hypertension with superimposed toxaemia. However, in many of these cases the final diagnosis could only be a presumptive one as these patients were seen for the first time as emergencies during the last trimester of pregnancy. Therefore all cases already studied, who had not been seen before the 20th week of gestation, were excluded from any further analyses, and cardiac catheterization was restricted thereafter to those patients in whom an adequate and reliable antenatal history had been obtained, and thus the diagnosis was made more accurate.

The technique of cardiac catheterization was identical with that used in the normal series (Hamilton, 1949a) and the patients were under similar basal conditions.

*The Standard denoting "Hypertension"*

The classification of the toxaemias of pregnancy is notoriously difficult, and even the maximum blood-pressures accepted as normal are disputed. We considered any blood-pressure reading taken under non-basal conditions attaining or exceeding either 140 systolic or 90 diastolic to be indicative of hypertension. Under basal conditions a blood-pressure sustained at not less than 140/80 was taken to indicate the presence of hypertension. This lower diastolic level was chosen as it was found that despite high diastolic pressures obtained in the wards a fall to below 90 was recorded in many cases once basal

conditions had been established. Many patients showing hypertension in the ward exhibited pressures within normal limits under basal conditions and they have been excluded from the analyses.

*Criteria of Diagnosis*

The diagnosis of pre-eclampsia was based on the presence of hypertension, with or without oedema or albuminuria commencing after the 20th week of gestation.

Essential hypertension was diagnosed in those patients who had a pressure of 140/90 on at least 2 occasions before the 20th week of gestation, the pressure being sustained at or about this level throughout the remainder of pregnancy. Some patients showed a slight mid-pregnancy fall in pressure, but not to a level below 130/80. Patients who showed a greater and more sustained mid-pregnancy drop were designated labile hypertension. Some cases of essential hypertension developed the signs of pre-eclampsia in the last weeks of pregnancy. The onset of the latter condition was heralded by a further rise of diastolic pressure (amounting to at least 20 mm. mercury) and the development of oedema and/or albuminuria. These cases were classified as having essential hypertension with superimposed pre-eclampsia.

The remaining patients had chronic nephritis. Albuminuria with or without hypertension was present before the 20th week of pregnancy. All but 1 of the 6 patients gave a history of previous acute nephritis, and urea clearance tests showed renal impairment.

*The Material*

The cases of pre-eclampsia have been divided into 2 groups. The first consisted of patients who showed hypertension, oedema and albuminuria, the last sign being present on 2 or more occasions in a catheter specimen. The second group consisted of patients who had had any of the following combination of signs: hypertension and albuminuria, hypertension and oedema or hypertension only. Generally speaking the cases in the first group were of greater clinical severity than those in the second group, but this ruling did not hold good in every case.

The material finally consisted of 25 cases of pre-eclampsia (14 Group I, and 11 Group II), 26 cases of essential hypertension, 9 cases of essential hypertension with superimposed toxaemia, 11 cases of labile hypertension and 6 cases of chronic nephritis, a total of 77 toxaemic patients.

*The Results*

The readings obtained for cardiac output and several associated variables have been analyzed and compared with each other and with those obtained in the normal series of 68 cases (Hamilton, 1949a).

### 1. *The Cardiac Output*

*Normal Series*

The cardiac output in normally pregnant women commences to rise during the 10th to 13th weeks of pregnancy and reaches a maximum of 5.73 litres per minute during the 26th-to-29th-weeks period. This represents an increase of 27 per cent above the non-pregnant level. The output has virtually returned to normal levels during the 38th to 40th weeks.

In these 68 cases the actual output varied from the mean curve by not more than 500 ml. in 74 per cent of cases. Thirteen per cent showed a decrease and 13 per cent an increase from the mean curve which, in each case, varied from 500 to 1,000 ml. (Table I).

*Pre-eclampsia, Group I. (Hypertension, Oedema and Albuminuria)*

In no case was the cardiac output within normal limits. The output was increased in 92.5 per cent and decreased in 7.5 per

cent of the cases. In approximately two-thirds of the cases the increase was of a moderate degree, amounting to 600 ml. to 1,500 ml. above the normal level for the period of gestation attained. The maximum increase recorded was 3,500 ml. and the maximum decrease 1,700 ml. (Table I).

*Pre-eclampsia, Group II (Hypertension and Oedema, or Hypertension and Albuminuria, or Hypertension alone)*

In this group 55 per cent of the cases had readings within the normal limits. The remaining cases were approximately evenly distributed between increased and decreased output. The maximum decrease was 2,000 ml. and the maximum increase 1,600 ml. (Table I).

*Essential Hypertension*

The output was within normal limits in 57 per cent of cases. In 12 per cent an increase in output was recorded, the maximum increase being 750 ml. In 31 per cent decrease was recorded, the maximum decrease being 1,700 ml. (Table I).

*Essential Hypertension + superimposed Pre-eclampsia*

The output was increased in all cases of hypertension with superimposed toxaemia. The increase was moderate in 56 per cent (600 to 1,500 ml.) and amounted to 1,600 to 2,500 ml. in 22 per cent, and to 2,600 to 3,500 in the remaining 22 per cent (Table I).

*Labile Hypertension*

Twenty-eight per cent of these cases had cardiac outputs within normal limits. The remaining 72 per cent showed an increase of from 500 to 2,500 ml. (Table I).

*Chronic Nephritis*

In 33 per cent of these patients the cardiac output was normal; in 67 per cent it was decreased by 600 to 1,600 ml. (Table I).

The cardiac output is within normal limits in cases of essential hypertension. Such cases thus seem to react in a similar manner to pregnancy as do normal patients. Cases of labile hypertension show a moderate increase in output.

Cases of severe pre-eclampsia, whether occurring in the previously normal or the previously hypertensive patient, have either a moderately or markedly raised cardiac output. The criterion of "severity" appears to be the presence of all three cardinal signs of toxaemia, namely hypertension, oedema, and albuminuria.

TABLE I

*Cardiac Output in Normal and Toxaemic Pregnancies*

*The range of variation of the cardiac output is shown as a percentage*

| CARDIAC OUTPUT | Normal Pregnancy (per cent) | Essential Hypertension (per cent) | P. E. T. Group I (per cent) | P. E. T. Group II (per cent) | Essential Hypertension & P.E.T. (per cent) | Labile Hypertension (per cent) | Chronic Nephritis (per cent) |
|---|---|---|---|---|---|---|---|
| Normal ±500 ml. | 74 | 57 | 0 | 55 | 0 | 28 | 33 |
| Increase 600–1,500 ml. | 13 | 12 | 57 | 18 | 56 | 36 | 0 |
| Increase 1,600–2,500 ml. | 0 | 0 | 28 | 9 | 22 | 36 | 0 |
| Increase 2,600–3,500 ml. | 0 | 0 | 7·5 | 0 | 22 | 0 | 0 |
| Decrease 600–1,500 ml. | 13 | 23 | 0 | 9 | 0 | 0 | 50 |
| Decrease 1,600–2,500 ml. | 0 | 8 | 7·5 | 9 | 0 | 0 | 17 |

The presence of albuminuria *per se* does not bear any relation to the level of the cardiac output. Cases showing mild and moderate degrees of pre-eclampsia (one or two signs only) have outputs which are on the whole within normal limits. They show approximately the same range of variation as the cases of essential hypertension.

Two-thirds of the patients with chronic nephritis in pregnancy have a decrease in cardiac output; the output in the remaining one-third is within normal limits.

In an attempt to determine what factor is responsible for the changes in cardiac output seen in cases of toxaemia of pregnancy the parts played by the numerator and denominator of the Fick equation have been studied.

### 2. *Oxygen Consumption*

In normal pregnancy the oxygen consumption rises steadily from the non-pregnant level of 211 ml. per minute to reach a maximum level of 251 ml. per minute during the third trimester (Hamilton, 1949a). In all cases of toxaemia the oxygen consumption was increased (Table II). In essential hypertension the increase was slight (262 ml. per minute). In labile hypertension and in pre-eclampsia, Group II, the increase was moderate (288 and 273 ml. per minute respectively), whereas in cases of pre-eclampsia, Group I, and essential hypertension with superimposed pre-eclampsia, the increase was even greater amounting to 291 and 296 ml. per minute respectively.

The cases of nephritis in pregnancy were catheterized during the second trimester and their mean oxygen consumption was 229 ml. per minute, i.e., within normal limits, the level during that period of gestation in a normal pregnancy being 234 ml. per minute.

### 3. *The Oxygen Arterio-venous Difference*

The oxygen A.V. difference in normal pregnancy remains at or about the normal non-pregnant level of 45 ml. per litre (Hamilton, 1949a) until the last 3 weeks of pregnancy when a marked increase is found (Table III). Each group of toxaemic cases has therefore been similarly analyzed, cases up to and including the 37th week of gestation and those during the 38th to 40th weeks being grouped together. The results are best seen in Table III. In essential hypertension the oxygen A.V. difference was increased in each group and the increase was of approximately the same magnitude at each period of gestation. In essential hypertension with superimposed pre-eclampsia the oxygen A.V. difference was depressed in both groups. In labile hypertension the oxygen A.V. difference was normal in the earlier weeks and increased in the last 3 weeks of pregnancy. This latter increase

TABLE II

*Oxygen Consumption in Normal and Toxaemic Pregnancies*

| | | Normal Pregnancy | Essential Hypertension | P. E. T. Group I | P. E. T. Group II | Essential Hypertension & P.E.T. | Labile Hypertension | Nephritis |
|---|---|---|---|---|---|---|---|---|
| Oxygen Consumption in ml./min. | 2nd. Trimester | 234 | — | — | — | — | — | 229 |
| | 3rd. Trimester | 251 | 262 | 291 | 273 | 296 | 288 | — |

TABLE III

*Oxygen Arterio-venous Difference in Normal and Toxaemic Pregnancies*

| | | Normal Pregnancy | Essential Hypertension | P. E. T. Group I | P. E. T. Group II | Essential Hypertension & P.E.T. | Labile Hypertension | Chronic Nephritis |
|---|---|---|---|---|---|---|---|---|
| $O_2$ A.V. Difference in ml./litre | 0–37 weeks | 43.99 | 52.8 | 51.3 | 52.9 | 41.5 | 44.6 | 50.7 |
| | 38–40 weeks | 55.2 | 61.8 | 48.7 | 59.2 | 47.9 | 62.75 | — |

paralleled that seen at the same period in essential hypertension.

In pre-eclampsia, Group II, the oxygen A.V. difference was increased in both gestational groups. In chronic nephritis there was a slight increase in oxygen A.V. difference.

Table IV contrasts the behaviour of the oxygen consumption, oxygen arterio-venous difference, and cardiac output in the several types of hypertensive toxaemia with the levels found in normal pregnancy. It will be observed that the increase in cardiac output in cases of both essential hypertension with superimposed pre-eclampsia and pre-eclampsia, Group I, is the result of an increased oxygen consumption being associated with a decreased oxygen arterio-venous difference. Patients with pre-eclampsia, Group II, do not differ from cases of normal pregnancy. In essential hypertension the oxygen consumption and oxygen arterio-venous difference are proportionately increased and the cardiac output remains unchanged.

To summarize, in cases of severe pre-eclampsia whether arising in a previously healthy patient or whether superimposed on a pre-existing hypertension the cardiac output is increased, often markedly so. Cases of mild pre-eclampsia and essential hypertension show a wider range of

TABLE IV.

*Oxygen Consumption, Oxygen Arterio-venous Difference, and Cardiac Output in Hypertensive Toxaemias as compared with Normal Pregnancy*

| Diagnosis | Oxygen Consumption | Oxygen Arterio-venous Difference | Cardiac output |
|---|---|---|---|
| Essential Hypertension | + | + | N |
| Labile Hypertension | + | N or + | + or N |
| Essential Hypertension + P.E.T. | + | − | + |
| Pre-eclampsia Group I | + | − | + |
| Pre-eclampsia Group II | N | N | N |
| Nephritis | N | + | − |

KEY. N = no change, + = increase, − = decrease from normal pregnant levels for the period of gestation.

variation in output than do normally pregnant women, but in each group in the majority of cases the output is within normal limits. In nephritis the cardiac output is usually depressed below normal limits and is never raised.

4. *The Right Auricular Pressure (R.A.P.)*

The R.A.P. was unaltered in all cases of toxaemia excepting nephritis (Table V). In 2 of the 6 cases of nephritis a positive pressure was recorded, one in a case 16 weeks pregnant (in hospital for observation only) and the other in a woman extremely ill at the 30th week of gestation with pre-eclampsia superimposed on the chronic nephritis. In the remaining 4 cases the R.A.P. was within normal limits.

5. *The Pulse Rate*

All patients were under basal conditions and the rate recorded was that attained after the cardiac catheter had been in position for 30 minutes. The basal pulse rate during the third trimester of normal pregnancy was 78 per minute. It was unaltered in cases of pre-eclampsia, nephritis and essential hypertension with superimposed pre-eclampsia. In cases of essential and labile hypertension the pulse rate was slightly increased (Table V).

6. *The Basal Blood-pressure*

The basal blood-pressure was the level attained after the catheter had been in position for 30 minutes. It was usually considerably lower than either non-basal ward readings or the first readings taken during catheterization. The average readings obtained are shown on Table V.

7. *The Stroke Volume*

The stroke volume in normal non-pregnant women is 63 ml. It is not altered from this level during the first trimester and last 3 weeks of pregnancy. It is increased to 72 ml. from the 14th to 37th weeks of normal pregnancy (Hamilton, 1949b). The toxaemic groups have been subdivided according to the period of gestation, 14 to 37 weeks and 38 to 40 weeks.

In essential hypertension a normal cardiac output was associated with an increased pulse rate, hence the stroke volume was decreased (Table V).

In essential hypertension with superimposed pre-eclampsia, on the other hand,

TABLE V

*R.A.P., Pulse Rate, Blood-Pressure and Stroke Volume in Normal and Toxaemic Pregnancies*

| | | Normal Pregnancy | Essential Hypertension | P. E. T. Group I | P. E. T. Group II | Essential Hypertension & P.E.T. | Labile Hypertension | Nephritis |
|---|---|---|---|---|---|---|---|---|
| R.A.P. in cm. Saline | | −3·5 | −4 | −2·5 | −3·5 | −3·5 | −4·3 | −0.5 |
| Pulse rate per minute | | 78 | 90 | 81 | 83 | 78 | 90 | 77 |
| Blood-Pressure (average) | | 114/72 | 140/90 | 138/89 | 132/92 | 152/102 | 129/87 | 140/90 |
| Stroke Volume in ml. | 14–37 weeks | 72 | ·57 | 72 | 66 | 86 | 72 | 60 |
| | 38–40 weeks | 62 | 49 | 78 | 60 | 84 | 54 | |

the output was increased but the pulse rate was normal and the stroke volume accordingly increased. In labile hypertension the stroke volume was within normal limits up to 37 weeks but was decreased in the 2 cases catheterized during the last 3 weeks of pregnancy (each of which had normal output). In pre-eclampsia, Group I, the stroke volume was normal in the 5 cases catheterized before the 38th week, and was increased in the 9 cases catheterized after the 38th week. In cases of pre-eclampsia, Group II, the stroke volume was slightly decreased in both gestation groups. In nephritis the stroke volume was decreased.

## Discussion

The presence of hypertension may be the first sign heralding the onset of one of the toxaemias of pregnancy. The hypertension may antedate conception or may appear for the first time during pregnancy. The latter type of hypertension may or may not disappear after delivery; the former type persists. Hypertension indicates the presence of some abnormality in the circulatory haemodynamics. Before the introduction of cardiac catheterization there was no method of directly assessing the impact of this abnormality on cardiac function. By means of cardiac catheterization, we can now measure accurately and directly the minute output of the heart under normal and pathological conditions. In normal pregnancy the cardiac output is increased during the greater part of gestation; the implication of this rise and of the terminal fall in output have already been discussed (Hamilton, 1949a).

The present investigation shows that the behaviour of the cardiac output varies with the type of toxaemia. In essential hypertension the cardiac output is within the normal pregnant limits though it shows a greater range of variation. This is not unexpected as non-pregnant patients with essential hypertension show no alteration in output (Richards, 1945) and it was reasonable to suppose that pregnant hypertensives would behave as did normally pregnant patients, providing that no other complicating factors arose. Cases of labile hypertension show wide variation in blood-pressure throughout pregnancy and a marked fall once basal conditions have been established. It is conceivable that these cases over-respond to adrenergic stimuli and they probably belong to the category of patients with a high cardiac output (McMichael and Sharpey-Shafer, 1944). It is reasonable to suppose that, as their hypertension becomes more stable, they will merge with the established essential hypertension group and that their cardiac outputs will then return to normal limits. Patients who have essential hypertension at the commencement of pregnancy are far more liable to develop superimposed pre-eclampsia than patients with normal blood-pressures (Browne and Dodds, 1942; Chesley and Annitto, 1947). All the 9 patients who had essential hypertension with superimposed pre-eclampsia had markedly increased cardiac outputs. This was also the case in those patients with pre-eclampsia who presented all three cardinal signs of the toxaemia. Patients who had only one or two signs of toxaemia showed very little alteration in the level of the cardiac output. The reason for this discrepancy is not obvious, but it is clear that in most cases of severe pre-eclampsia, whether arising *de novo* or whether superimposed on a pre-existing hypertension, the cardiac output is markedly increased, indicating that a major alteration has occurred in the cardiovascular haemodynamics. In less severe cases of pre-eclampsia and in labile hypertension the cardiac output shows a greater range of

variation than is found in normal pregnancy.

Cases of chronic nephritis in pregnancy show a marked decrease in cardiac output, though these results must be regarded as merely suggestive, as the number of cases was small.

## Summary

1. The cardiac output in 77 cases of toxaemia of pregnancy has been investigated using the method of cardiac catheterization. The results have been compared with those found in a similar group of normally pregnant patients investigated under identical conditions.

2. In the 26 cases of essential hypertension the cardiac output was unaltered. In 11 cases of labile hypertension the cardiac output was moderately increased in 72 per cent. In 9 cases of essential hypertension with superimposed pre-eclampsia the cardiac output was increased in 100 per cent.

3. Cases of pre-eclampsia showing all three cardinal signs (14 cases) had a raised cardiac output in 92.5 per cent. Eleven cases of pre-eclampsia with only one or two signs had cardiac outputs within normal limits.

4. In the 6 cases of chronic nephritis in pregnancy decreased outputs were found in 67 per cent.

5. The factors contributing to the determination of the cardiac output, oxygen consumption and oxygen arterio-venous difference, have been anlyzed in each group of cases.

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