THE THYROID TREATMENT OF ESSENTIAL HYPERTENSION
REPORT ON 334 CASES

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In an earlier communication I postulated a disturbance in adrenal-thyroid balance in the direction of thyroid insufficiency as the basic factor in the causation of essential hypertension. Since then several developments have strengthened the validity of this concept.

In the first place the blood-pressure-raising substance of the adrenal gland has been shown to be noradrenalin. All who have investigated its properties have found that it consistently raises the diastolic and systolic blood pressures. Moreover noradrenalin has been identified as the sympathetic activator or mediator which was of such vital concern to Cannon and his associates. Von Euler considers it to be 'the dominating adrenergic neurohormone'.

Next we have the important observation of Barnett and his co-workers that a number of subjects while receiving noradrenalin infusions developed a swelling of the thyroid gland, which subsided shortly after the infusion was stopped. In 1937, in a case of phaeochromocytoma, Strombeck and Hedburg found that the paroxysms of hypertension were accompanied by a swelling of the thyroid gland which also subsided when the attack was over.

These observations throw light on the pathogenesis of Graves' disease. Here, swelling of the gland often follows some terrifying experience. Physiologically this means the pouring into the blood stream not only of adrenalin but, as we may now say, also of noradrenalin. From this and also because sympathetic over-activity is a salient feature of this disease it seems reasonable to infer that the enlargement of the thyroid gland is a reaction to over-activity of the adrenal medulla.

These facts taken in conjunction with the vasoconstrictor and diastolic-pressure-raising effect of noradrenalin and the vasodilator and the diastolic-pressure-lowering effect of thyroid extract, indicate that in their action on the blood-pressure the adrenal medulla and the thyroid gland are antagonistic. They confirm my view that in the aetiology of essential hypertension thyroid insufficiency is of fundamental importance.

TREATMENT
I. ANALYSIS OF RESULTS

I began to treat essential hypertension with thyroid extract in November 1948, and in March 1950 reported on the first 50 cases. I am now able to add to these a further 284 making a total of 334 cases. Of these 229 or 69% responded favourably. The criteria for favourable response were relief of symptoms and a clearly defined fall in the blood pressure. Symptomatic relief alone was not regarded as a positive response.

The patients received no treatment apart from thyroid extract. All were ambulatory and were carrying on their daily tasks while receiving treatment.

The results may be grouped under three heads based on the degree to which the blood pressure fell under treatment. Taking the arbitrary figure of 130/90 mm Hg as the upper limit of normal, the first group consists of cases where the blood pressure fell to normal; the second where it fell to a level between the original reading and the normal figure, and the third where there was no fall at all (Table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>Blood Pressure</th>
<th>No. of Cases</th>
<th>Percentage of Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Fall</td>
<td>46</td>
<td>14</td>
</tr>
<tr>
<td>II</td>
<td>Fall to intermediate level</td>
<td>183</td>
<td>55</td>
</tr>
<tr>
<td>III</td>
<td>No fall</td>
<td>105</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td></td>
<td>334</td>
<td>100</td>
</tr>
</tbody>
</table>

2: CASE REPORTS

In the interests of brevity a great many blood pressure readings and details as to dosage have been omitted from the reports which follow. Fuller details of the progress of these cases will appear in a publication which is pending.

GROUP 1.

Return of blood pressure to normal levels with relief of symptoms.

Examples:

Case 1. Mrs. E. B. Age 65.
Complaints: Giddiness, headaches, shortness of breath.
History: Occasional headaches and giddiness in the past, but continuous for the last 2 to 3 months. Headaches occipital. Shortness of breath on exertion only. No angina of effort.

 returned high blood pressure according to out-patient records as far back as 17 December 1943.

Date: Blood Pressure Treatment and Results

17 December 1943 210/100. Pulse 72. Thyroid extract gr. 5.
10 January 1951 200/100. Pulse 74. Blood cholesterol 240 mg. per 100 c.c.

24 January 1951 160/78. Blood cholesterol 170 mg. per 100 c.c. Giddiness gone; feels better. No headaches in last 14 days. Feeling very well.
7 March 1951 164/80. Complains of palpitation. Thyroid gr. 3. 5 days in the week.
28 March 1951 130/70. Pulse 80. Thyroid gr. 3. Stop thyroid.
20 August 1951 120/54. Pulse 60. Blood cholesterol 210 mg. per 100 c.c.

3 September 1951 124/70. Pulse 60. No thyroid.
17 September 1951 150/70. Pulse 64. Thyroid gr. 3.
15 October 1951 140/70. Pulse 60. Thyroid gr. 3.
7 January 1952 106/58. Pulse 60. Feels well. Stop thyroid.
Case 2. Mrs. H. M. P. Age 27.

Complaints: Headaches and giddiness for past 5 years. Numbness of hands and feet.

History: Headaches and attacks of giddiness have been getting progressively worse over the last 5 years. Has been pregnant 5 times. Had 2 miscarriages, 3 still-births; labour induced because of high blood-pressure.

Examination: Nil, except elevated blood pressure.

**Blood Pressure in mm. Hg, etc.**

<table>
<thead>
<tr>
<th>Date</th>
<th>Treatment and Results</th>
<th>Blood Pressure in mm. Hg, etc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 January 1951</td>
<td>Thyroid gr. 3.</td>
<td>180/120. Pulse 80.</td>
</tr>
</tbody>
</table>
| 7 February 1951 | Headaches less severe; giddiness less. Num­
|                 | bness of hands and feet gone. Very tired and shaky for last five days. Thyroid gr. 2. |
| 14 February 1951| Headaches gone. Giddi­
|                 | ness gone. No symp­tionts of overdos­
|                 | age. Thyroid gr. 2. |
| 28 February 1951| Thyroid gr. 2.        | 148/88. Pulse 80.             |
| 6 June 1951     | No recurrence of head­
|                 | aches and giddiness since they dis­
|                 | appeared four months ago. Thyroid gr. 3. |
| 15 October 1951 | Feeling very well. Stop thyroid. |
| 12 December 1951| Feels well. Thyroid gr.
|                 | 3. |
| 23 January 1952 | Feels well. Thyroid gr.
|                 | 3. |

Case 3. Mrs. E. A. S. Age 68.

Complaints: Head-noises and deafness. Headaches. No giddiness now, but was giddy ten years ago. No angina of effort.

Examination: Brachials thickened; blood pressure elevated.

**Blood Pressure in mm. Hg, etc.**

<table>
<thead>
<tr>
<th>Date</th>
<th>Treatment and Results</th>
<th>Blood Pressure in mm. Hg, etc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 September 1950</td>
<td>Thyroid gr. 5.</td>
<td>204/106. Blood cholesterol 180 mg. per 100 c.c.</td>
</tr>
<tr>
<td>13 September 1950</td>
<td>Thyroid gr. 5.</td>
<td>180/100. Blood cholesterol 210 mg. per 100 c.c.</td>
</tr>
<tr>
<td>27 September 1950</td>
<td>Thyroid gr. 5.</td>
<td>172/90. Blood cholesterol 210 mg. per 100 c.c.</td>
</tr>
<tr>
<td>25 October 1950</td>
<td>Thyroid gr. 3, 5 days in the week.</td>
<td></td>
</tr>
<tr>
<td>27 November 1950</td>
<td>Thyroid gr. 3, 5 days in the week.</td>
<td></td>
</tr>
<tr>
<td>8 January 1951</td>
<td>Thyroid gr. 3, 5 days in the week.</td>
<td></td>
</tr>
<tr>
<td>19 February 1951</td>
<td>Feeling 'very well in herself'. Thyroid gr. 3, 5 days in the week.</td>
<td></td>
</tr>
<tr>
<td>30 April 1951</td>
<td>Thyroid gr. 3, 5 days in the week.</td>
<td></td>
</tr>
<tr>
<td>28 May 1951</td>
<td>Thyroid gr. 3, 5 days in the week.</td>
<td></td>
</tr>
<tr>
<td>25 June 1951</td>
<td>Head noises still present</td>
<td></td>
</tr>
</tbody>
</table>
| 23 July 1951      | States that for the last two months has ex­
|                   | perienced pain in the chest on walking. This is so severe that she has to stop. The pain is relieved by rest. Stop thyroid. |

Case 4. Mrs. G. C. N. Age 53.


History: Has had a high blood pressure for about twenty years. Condition began with frequent nose bleeds. Five days before she saw me, just before midnight, suddenly felt her right arm and face become numb. Tongue felt heavy and speech was slurred. This lasted for about half-an-hour and then passed off. No angina of effort. No renal disease as far as she knows.


**Blood Pressure in mm. Hg, etc.**

<table>
<thead>
<tr>
<th>Date</th>
<th>Treatment and Results</th>
<th>Blood Pressure in mm. Hg, etc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>9 January 1951</td>
<td>Thyroid gr. 2.</td>
<td>270/154. Pulse 104.</td>
</tr>
<tr>
<td>23 January 1951</td>
<td>Thyroid gr. 2.</td>
<td>234/134. Pulse 110.</td>
</tr>
<tr>
<td>13 February 1951</td>
<td>Better in every way. No headaches except with her periods but these are 'different'. Giddiness very slight now. Is sleeping very well. Thyroid gr. 2.</td>
<td></td>
</tr>
<tr>
<td>5 April 1951</td>
<td>No petechiae.</td>
<td>224/124. Pulse 100.</td>
</tr>
</tbody>
</table>
| 25 May 1951       | Improvement main­
|                   | tained. More ener­
|                   | getic. Not short of
|                   | breath. No longer
|                   | bruises easily. 'First
|                   | time you took my
|                   | blood pressure my
|                   | arm was purple
|                   | for days afterwards'. Thyroid gr. 2. |
| 18 August 1951    | Thyroid gr. 2.        | 200/112. Pulse 90.            |

Case 5. Mr. S. J. S. Age 77.

Complaints and History: Legs ache all day and cramp every night for past three months. For past three weeks has noticed that after walking about fifty paces, gets a severe pain in the left calf which forces him to stop walking. On resting pain goes away.

105 out of 334

**Case 7. Mrs. A. J. K. J. Age 58.**

**Complaints:** Headaches. Giddiness. Thirst. Slight polyuria.

**History:** All symptoms of about a year's duration. For the past 2 months headaches have been severe and of almost daily occurrence.

**Examination:** Brachials thickened and tortuous. Blood pressure elevated. Urine; sugar ++ + (brown to Benedict's test).

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**Case 6. Mr. H. J. v. d. W. Age 47.**

**Complaints:** Headaches, giddiness, noises in the ears, palpitation, cold feet, insomnia. He is irritable and bad tempered. Majority of symptoms present since 1942.

**Examination:** Left ventricular enlargement, heaving cardiac impulse. Thickened brachials and elevated blood pressure.

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**Date** | **Blood Pressure in mm. Hg, etc.** | **Treatment and Results** | **Case 7. Mrs. A. J. K. J. Age 58.**
---|---|---|---
16 August 1950 | 200/100. Pulse 88. | Thyroid gr. 5. | **Date** | **Blood Pressure in mm. Hg, etc.** | **Treatment and Results** | **14 May 1952** | 228/130. Pulse 112. | Sugar ++ +. | **18 October 1950** | 170/112. Blood cholesterol 200 mg. per 100 c.c. | Thyroid gr. 3, five days
30 August 1950 | 210/104. Pulse 86. | Blood cholesterol 300 mg. per 100 c.c. | | | | | | | | | | |
20 September 1950 | 168/80. Pulse 86. | Thyroid gr. 5, five days in the week. | | | | | | | | | | |
11 October 1950 | 158/70...0. Pulse 88. | Feels weak and shaky. Thyroid gr. 3. | | | | | | | | | | |
1 November 1950 | 160/80. Pulse 82. | States that for the past month aching in limbs has gone completely. Cramps have also gone. Feels 'much better bodily'. Thyroid gr. 4. | | | | | | | | | | |
20 December 1950 | 168/84. Pulse 80. | Thyroid gr. 4. | | | | | | | | | | |
17 January 1951 | 150/80. Pulse 80. | States walking better and farther but feels weak. Thyroid gr. 3. | | | | | | | | | | |
13 February 1951 | 160/80. Pulse 80. | Thyroid gr. 2. Walking much better. Has walked from hospital to centre of town (about one mile), with only one stop. Feeling well. No further improvement in exercise tolerance. Thyroid gr. 2. | | | | | | | | | | |
22 February 1951 | 174/90. Pulse 84. | | | | | | | | | | |
9 May 1951 | 166/86. Pulse 88. | | | | | | | | | | |
21 May 1952 | 142/80. Pulse 76. | | | | | | | | | | |

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**Date** | **Blood Pressure in mm. Hg, etc.** | **Treatment and Results** | **Case 6. Mr. H. J. v. d. W. Age 47.**
---|---|---|---
30 April 1952 | 254/174. Pulse 108. | Thyroid gr. 3. | **Date** | **Blood Pressure in mm. Hg, etc.** | **Treatment and Results** | **14 May 1952** | 228/112. Pulse 104. | Sugar ++ +. | **18 October 1950** | 170/112. Blood cholesterol 180 mg. per 100 c.c. | Thyroid gr. 3, five days
12 December 1951 | 170/120. Pulse 80. | | | | | | | | | | |
11 June 1952 | 226/140. Pulse 104. | Sugar ++ +. | | | | | | | | | | |

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**Blood Pressure in mm. Hg, etc.** | **Treatment and Results** | **Case 6. Mr. H. J. v. d. W. Age 47.**
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12 July 1950 | 184/104. Pulse 120. | | | | | | | | | | |
2 October 1950 | 242/160. Pulse 110. | | | | | | | | | | |
1 November 1950 | 205/138. Pulse 90. | | | | | | | | | | |
29 November 1950 | 192/128. Blood cholesterol 190 mg. per 100 c.c. | | | | | | | | | | |
10 January 1951 | 184/124. Blood cholesterol 190 mg. per 100 c.c. | | | | | | | | | | |
16 May 1951 | 216/140. | | | | | | | | | | |
13 June 1951 | 184/124. | | | | | | | | | | |
11 July 1951 | 166/110. | | | | | | | | | | |
12 December 1951 | 170/120. Pulse 80. | | | | | | | | | | |
23 January 1952 | 170/120. Pulse 80. | | | | | | | | | | |

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**Case 6. Mr. H. J. v. d. W. Age 47.**

**Complaints:** Headaches, giddiness, noises in the ears, palpitation, cold feet, insomnia. He is irritable and bad tempered. Majority of symptoms present since 1942.

**Examination:** Left ventricular enlargement, heaving cardiac impulse. Thickened brachials and elevated blood pressure.

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**Examination:** Elevated blood pressure and tachycardia.

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**GROUP III.**

No appreciable drop in blood pressure: 105 out of 334 cases or in 31%.

**Examples:**

**Case 8. Mrs. B. C. B. Age 35.**

**Complaints:** Headaches—occipital, occurring especially with her periods. Noises in the ears. Cold hands and feet. Insomnia.

**History:** 1939—at fifth month of first pregnancy had pyelitis and was also found to be hypertensive. Had a fit in later months of pregnancy. Delivered a full term live baby.

1943—Unventful pregnancy.

1949—Again pregnant. In third month; pyelitis and hypertension. Abdominal hysterectomy and sterilization. Under care of genito-urinary specialist for eight months.

**Examination:** Elevated blood pressure and tachycardia.

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**Diagnosis:** Renal hypertension. (Chronic pyelonephritis).
Case 9. Mrs. H. M. Age 51.


History: Small stroke Dec. 1948. Another Dec. 1949. Has had a high blood pressure to her knowledge since 1944. Severe attack of scarlet fever at the age of 25; in bed for 6 months. Father died after a heart attack. Mother died after she had two strokes. A brother died at the age of 33 from hypertension and renal failure.

Examination: Left ventricular enlargement. Blood pressure elevated. Fundal exudates. Renal function test; concentration and dilution tests revealed a specific gravity, fixed at 1010.

Date Blood Pressure in mm. Hg, etc. Treatment and Results
21 March 1950 ... 250/160 ... Thyroid gr. 5.
28 March 1950 ... 235/150 ... Thyroid gr. 10.
12 April 1950 ... 235/145 ... Symptoms of overdosage. Thyroid gr. 5.
3 May 1950 ... 236/144 ... No symptoms of overdosage. Sleeping better. Thyroid gr. 5.
28 May 1950 ... 235/154 ... Feeling better. Thyroid gr. 8.
5 July 1950 ... 230/150 ... Symptoms of overdosage. Stop thyroid.

Diagnosis: Renal hypertension (Chronic glomerulo-nephritis or Nephrosclerosis or both).

Note: (1) Thyroid Thyroideum siccum. The stated dose was usually taken at night before retiring.

(2) Blood cholesterol estimations were undertaken in only small percentage of the cases. They seem to indicate that thyroid extract lowers the blood cholesterol level in essential hypertension.

3. Comment

(a) Relationship of Essential Hypertension to Renal Hypertension. Among the 17 cases in my first series \(^1\) which failed to respond, there were 4 where there could be no doubt as to the cause of the hypertension. They were respectively, a case of polycystic kidneys, one of chronic glomerulo-nephritis, one of unilateral hypoplastic kidney \(^2\) (unilateral pyelonephritis) and one of unilateral hydronephrosis. The failure of these to react made me suspect that in renal hypertension, thyroid medication will not bring down the blood pressure. Further experience has confirmed this view. Moreover, this is what one would expect, for the mechanism whereby the blood pressure is elevated in renal hypertension is quite different from the "sympathetic" mechanism mediated by noradrenalin.

Since the time of Richard Bright numerous observations have established the association of renal disease with hypertension, but it was not until 1934 that the work of Goldblatt \(^3\) established the nature of the relationship. He and the South American School of Houssay and Braun-Menéndez \(^4\) showed conclusively that the cause of renal hypertension was renal ischaemia. This discovery explained for the first time why in perhaps half the patients with demonstrable renal disease no hypertension is found. In these cases the disease process, whatever it be, has not produced a diminution in the renal blood flow.

It is well known that essential hypertension will in time bring about a narrowing of the renal vessels and ischaemia. In fact it would be correct to say that essential hypertension is the commonest cause of renal ischaemia and therefore of renal hypertension. Thus the majority of cases of essential hypertension will be complicated by varying degrees of renal hypertension. As thyroid extract does not bring down the blood pressure in the latter the response in each case will depend on the degree to which the mechanism mediated by noradrenalin is responsible for its elevation.

Reverting now to the analysis of the results of treatment, Group 1, one may say, consists of cases of "pure" essential hypertension. The response to treatment here is complete. In Group II are the cases in which both the "sympathetic" and the renal mechanisms are responsible for elevating the blood pressure. These constitute the "mixed" type and response to thyroid medication is intermediate and proportional to the extent that thyroid insufficiency is responsible for elevating the blood pressure. Group III consists of cases of "pure" renal hypertension, the majority of which have been caused by ischaemia resulting from essential hypertension.

(b) Essential Hypertension and Atheroma. Atheroma and hypertension are closely associated. Firstbrook \(^5\) quoting Wilens states: 'severe athero-sclerosis is about twice as common in hypertensives as in non-hypertensives of the same age, sex and adiposity'. Is the deposition of cholesterol in blood vessels a manifestation of endocrine imbalance? In this context the elevation of the blood cholesterol level in hypothyroidism and in essential hypertension \(^6\) and its depression in hyperthyroidism are significant.

A possible link between hypertension and atheroma could be an excessive intake of fat. This may cause an added burden to be placed upon a constitutionally weak thyroid gland in much the same way as an excessive intake of carbohydrate overburdens a constitutionally inferior islet-cell system in the potential diabetic. If this is so, have we in thyroid extract, which causes a fall in blood cholesterol, a substance which will prevent or remove atheroma?

(c) Therapeutic Details. I would like at the outset to reiterate \(^7\) that we must overcome our thyrophobia if we are to treat essential hypertension adequately. If allowance is made for certain clearly defined contra-indications I am satisfied that we have nothing to fear from the prolonged administration of thyroid extract. The fear that it might damage the heart in some mysterious way is based on the observation that in long-standing Graves' disease the heart is often damaged. This fact, however, has been misinterpreted. Graves' disease is as much a manifestation of adrenal medullary overactivity as it is of thyroid overaction and from our knowledge of the action of adrenalin and noradrenalin it is far more likely that the heart is injured by these hormones than by an excess of thyroid secretion.

The first point of practical importance is the choice of preparation. \(^8\) Thyroid extracts vary in potency, some because of deficiencies in hormone content and others because they are not completely absorbed. I have found the following preparations of thyroideum siccum to be...
The essence of treatment is to discover by trial and error what the maintenance dose is to be. The object is not to give the largest possible dose. Remember that we are attempting to restore a balance disturbed in the direction of hypothyroidism. Overdosage will in time produce symptoms as distressing as those we are trying to alleviate.

In some cases the blood pressure after having come down will rise again. Two factors may be responsible:

1. The patient may have been subjected to some added emotional stress, or
2. The dose may be excessive.

If a patient whose blood pressure has been adequately controlled is subjected to some added emotional stress such as that associated with a motor accident, a financial loss, domestic strife or the death of a member of the family, the blood pressure rises and symptoms recur. The position is analogous to what occurs in a case of diabetes mellitus controlled by insulin when subjected to similar stresses. The procedure here is to increase the dose and to advise patients to do this themselves if the period of stress is prolonged.

That excessive dosage might be the cause of the elevation of blood pressure after it had first come down, was an explanation which eluded me for a long time. It occurred infrequently (in about 10 instances) and usually after the patient had been on the determined maintenance dose for a long period—3 to 6 months or even longer. My first reaction to the rise in the pressure was to increase the dose. This caused it to rise still further and the symptoms to be aggravated. On stopping treatment the pressure fell within 5 days and remained down for at least a fortnight with relief of symptoms. The best explanation, and one in accord with the evidence of adrenal-thyroid antagonism, is that an excessive dose given over a long period results in adrenal medullary overactivity—a rebound phenomenon. It appears to be due to the maintenance dose being a little in excess of what it should be. After stopping treatment my procedure is to observe the blood pressure until it begins to rise again and then to give a dose just below the original maintenance dose. It is also helpful here to institute a 1- or 2-day break every week.

It is possible that the phenomenon will occur more frequently if cases are observed for longer periods. It may also occur sooner if one is careless about dosage. Careful attention to the pulse-rate and a closer approximation to the maintenance dose by the use of half-grain tablets should obviate this occurrence.

The remaining points of therapeutic importance might be summarized as follows:

1. As already mentioned a significant drop in the blood pressure is not to be expected in cases of 'pure' renal hypertension. As essential hypertension is the chief cause of renal hypertension and as hypertension is the chief cause of arteriosclerosis, the paramount importance of early diagnosis and treatment is apparent.

2. Cases of essential hypertension complicated by renal hypertension will respond in proportion to the extent that the hypertension is due to thyroid insufficiency. This can only be determined by therapeutic trial.

3. Essential hypertension complicated by an extreme degree of renal ischaemia will give rise to 'malignant' hypertension. Such cases should not respond to thyroid medication.

4. Once the heart muscle has failed there is little one can do. Left-sided congestive failure, right-sided congestive failure, complete heart-block, gross cardiac enlargement and coronary thrombosis are contra-indications. Angina of effort is an important contra-indication because the blood supply to the heart muscle is dependent on the blood pressure. With a fall in blood pressure, attacks occur more readily. Moreover, there is here the added danger of precipitating coronary thrombosis.

Moderate enlargement of the heart, auricular fibrillation, premature beats and bundle-branch block are not contra-indications.

5. Cases of essential hypertension with predominantly cerebral symptoms respond particularly well even after two or three cerebral vascular complications.

6. Diabetes mellitus is not a contra-indication.

SUMMARY

1. In the regulation of blood pressure the adrenal medulla and the thyroid gland have antagonistic actions.

2. On the assumption that thyroid insufficiency is the basic factor in the causation of essential hypertension, 334 cases of hypertension were treated with thyroid extract. About 70% responded favourably.

3. Renal hypertension does not respond to thyroid treatment.

4. The value of thyroid extract in the treatment of essential hypertension is confirmed.

REFERENCES