BLOOD PRESSURE DURING EXERCISE AND THE EFFECT OF HEXAMETHONIUM

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This paper is concerned with the effect of exercise on the blood pressure and the modification of this effect by hexamethonium bromide. It is well known that the methonium compounds can produce a fall in the blood pressure of many hypertensive subjects when lying down. This fall, however, is variable and inconstant. In normal persons, the methonium compounds do not produce a fall in the basal blood pressure taken in the supine position (Conway, 1953). In all persons, normal and hypertensive, methonium compounds produce a postural fall in the blood pressure. This postural hypotension has, for the most part, been regarded as an undesirable side-effect of methonium therapy but some have attempted to turn it to good account; for example, the head of the bed has been raised on blocks as a routine part of hexamethonium treatment of hypertension (Shirley Smith, 1953).

By taking blood pressure recordings in the lying and standing positions, it was found that hexamethonium bromide had, in many subjects, only a postural effect. If this postural effect was only present when the person was standing still and passed off on exercise—and this seemed a likely *a priori* supposition—then the postural hypotension would obviously be of no value but merely an unpleasant side-effect likely to cause fainting in the erect position, or even to precipitate thrombosis. If, however, a hypotensive effect persisted on exercise—that is when the patient was upright and about his daily work—then this so-called side-action should constitute a most significant factor in the treatment of hypertension by the methonium compounds. It, therefore, seemed logical to study the effect of exercise on the blood pressure of hypertensive persons before and after treatment with methonium compounds.

METHOD AND CLINICAL MATERIAL

The blood pressure has been recorded while a quarter of a mile was bicycled on an ergometer with one arm supported on a rest. The measurement was made in the usual way by the auscultatory method using a Riva-Rocca sphygmomanometer. The subject was first rested, sitting on the bicycle till readings were constant, and the blood pressure was then recorded twice during the exercise while the work was done at a smart rate, just short of inducing distress of breathing or fatigue. Immediately after exercise the blood pressure was taken again and thereafter at one-minute intervals until the influence of the exercise on the blood pressure had passed off.

These studies were conducted upon 30 normal and 45 hypertensive subjects, who were grouped as follows.

- (1) Young normal subjects.
- (2) Elderly normal subjects.
- (3) Subjects with benign essential hypertension (mild or moderate).
- (4) Subjects with essential hypertension of severe degree.
- (5) Subjects with essential hypertension modified by hexamethonium bromide.

RESULTS

Young Normal Subjects. All showed a rise of systolic pressure of 10–30 mm. Hg, with no change or a slight fall in the diastolic pressure. The blood pressure returned to normal in three or four minutes (Fig. 1).

Elderly Normal Subjects. All the elderly normal subjects studied were in hospital for minor surgical procedures. Generally the response of the blood pressure to exercise was essentially the same as in young persons, but in three elderly men it was exaggerated, the blood pressure rising as much as 80 mm. Hg above the resting level (Table I). It was found that these three had, in common, a high pulse pressure. In the absence of aortic incompetence or lowered peripheral resistance, a high pulse pressure must be due to

FIG. 1

FIG. 2

FIG. 3

FIG. 1.*—Figure to show the range of response of the blood pressure to exercise in normal young persons.

FIG. 2.—Three exercise tests to show the constancy of the blood pressure response to exercise in a case of mild hypertension.

FIG. 3.—Effect of exercise on the blood pressure in a case of severe hypertension.

TABLE I*
BLOOD PRESSURE RESPONSE TO EXERCISE TEST IN MEDIAL SCLEROSIS

Subject	Age	R	DE	DE	IAE	IM	2M	3M
C/1	65	150/60	220/60	220/60	200/60	190/60	170/60	150/60
C/2	60	160/70	210/60	210/60	200/60	180/65	170/70	160/70
C/3	67	170/80	250/65	250/65	260/65	260/65	250/60	220/70

* In all the tables and figures the following symbols have been used:
R=resting. DE=during exercise. IAE=immediately after exercise. M=minute. HMB=hexamethonium bromide. PVP=polyvinylpyrrolidone. For exercise, sys.=systolic, dias.=diastolic. Figures along abscissæ refer to blood pressure in mm. Hg.

rigidity of the arteries (as opposed to arteriolar narrowing), and these subjects should therefore be considered as examples of medial sclerosis, although they had no other physical signs of this condition.

Subjects with Benign Essential Hypertension (mild to moderate). In benign essential hypertension of mild or moderate degree, the blood pressure rise on exercise tended to be more pronounced than in normal persons (Table II). This is illustrated in Fig. 2 which also shows the constancy, for any patient, of the blood pressure response to exercise, where the clinical state is unchanged. The readings, in the case illustrated, were taken at intervals of a month apart.

TABLE II
BLOOD PRESSURE RESPONSE TO EXERCISE TEST BEFORE AND AFTER HMB IN MILD TO MODERATE
ESSENTIAL HYPERTENSION

Subject	R	DE	DE	IAE	1M	2M	3M
D/1 Before HMB After HMB	195/105 150/85	240/110 160/85	270/110 170/85	270/110 170/75	250/110 160/85	230/110 155/85	200/105 145/80
D/2 Before HMB After HMB	170/110 150/100	210/100 170/100	210/100 170/100	210/100 180/100	180/100 160/100	160/100 150/100	160/100 150/100
D/3 Before HMB After HMB	190/110 130/70	240/120 160/80	270/130 160/80	240/120 160/85	190/110 170/70	180/110 160/65	180/110 140/60
D/4 Before HMB After HMB	190/120 170/90	230/120 180/100	230/120 180/100	240/120 180/100	220/95 180/100	210/95 180/100	195/110 180/100
D/5 Before HMB After HMB	210/110 160/110	230/120 170/115	230/120 180/115	230/120 180/115	230/120 170/110	200/110 170/110	175/105 160/110

Subjects with Essential Hypertension of Severe Degree. In these cases the pattern of blood pressure response to exercise was found to be fundamentally altered. There was either no rise of systolic blood pressure on exercise (Fig. 3 and Table III), or in the most severe cases the blood pressure, in fact, fell during exercise with a marked post-exertional hypertension (Fig. 4). These patients were not in heart failure.

TABLE III
BLOOD PRESSURE RESPONSE TO EXERCISE TEST BEFORE AND AFTER HMB IN SEVERE ESSENTIAL HYPERTENSION

Subject	R	DE	DE	IAE	1M	2M	3M
E/1 Before HMB After HMB	190/130 160/120	180/130 170/120	180/130 170/120	190/135 170/120	180/130 150/110	180/130 145/110	180/130 155/115
E/2 Before HMB After HMB	180/110 130/90	180/110 130/90	180/110 155/90	190/110 155/90	180/110 150/90	170/100 140/90	170/100 130/90
E/3 Before HMB After HMB	230/140 180/120	230/140 185/120	230/140 190/110	240/140 195/110	230/140 185/110	230/140 185/120	230/140 180/120
E/4 Before HMB After HMB	200/110 150/100	200/120 150/100	200/120 150/100	200/120 150/100	200/120 150/100	200/120 150/100	200/120 150/100
E/5 Before HMB After HMB	220/150 70/50	230/150 100/80	230/150 100/80	230/150 90/70	230/150 70/50	230/140 70/50	230/150 70/50

FIG. 4.—Blood pressure response to exercise test in two patients, F/1 and F/2: both cases of pre-malignant hypertension with initial readings of 260/160 and 280/180 respectively.

FIG. 5 and 6.—Tests to show the blood pressure response to exercise before and after treatment in two cases of essential hypertension. X=before treatment. X1= 45' after HMB 60 mg. in PVP. Y=before treatment. Y1=4 hours after 50 mg. HMB in PVP. Y2= 8 hours after 50 mg. HMB in PVP.

It will be seen, in Table III, that some of the patients before treatment with hexamethonium bromide (E/2 and E/4), had diastolic pressures of only 110 mm. Hg yet they were still classed in the severe group. This followed a period of bed rest in hospital, and they were graded as severe on other criteria than the diastolic blood pressure alone.

Subjects with Essential Hypertension Modified by Hexamethonium Bromide. Hexamethonium bromide has been shown to depress, not only the resting blood pressure, but also, the peak blood pressure figure on exercise. The shape of the curve was, however, unchanged (Fig. 5 and 6). In a few subjects a marked post-exertional hypotension was noted. It was not related to treatment with hexamethonium bromide, and in one case it occurred before, and in another case only after treatment (Fig. 7 and 8).

With one exception, the *pattern* of blood pressure response to exercise was unaltered by hexamethonium bromide because the peak blood pressures were lowered in relation to the reduction of the resting blood pressures. The one exception in which the peak blood pressure on exercise was not suppressed by hexamethonium bromide is shown in Fig. 9. It was seen that, although this patient had essential hypertension with a raised diastolic pressure of 110 mm. Hg (before prolonged bed rest in hospital had brought it down to 90), there was a very high pulse pressure. He had other evidence of medial sclerosis with thickened tortuous brachial arteries. It is presumed that the rigid arteries, obviously uninfluenced by a ganglion-blocking agent, were responsible for the failure of the peak blood pressure to be lowered by hexamethonium bromide.

DISCUSSION

Much work on the relationship of exercise to blood pressure has been done, but it has mainly consisted of blood pressure readings taken after, rather than during, exercise. In a standard textbook of physiology (Best and Taylor, 1950) it has been assumed, following the work of Cotton *et al.*

FIG. 7

FIG. 8

FIG. 9

FIG. 7 and 8.—Tests to show the effect of exercise on the blood pressure in two cases of benign hypertension and the phenomenon of post-exertional hypotension. X=before treatment. X1=2½ hours after 50 mg. HMB in PVP. Y=before treatment. Y1=3 hours after 50 mg. HMB in PVP.

FIG. 9.—Test to show the effect of exercise on the blood pressure in a case of medial sclerosis. X=before HMB. X1=3 hours after 80 mg. HMB in PVP.

(1917), that there is a rise of blood pressure during exercise, an immediate post-exertional fall to, or below, the resting pressure, followed by a rise to the figure obtaining during exercise and a subsequent fall. Cotton *et al.* believed that the post-exertional fall was due to the formation of a potential unfilled venous reservoir which, until it filled and started to overflow, lowered the blood pressure by reducing the venous return to the heart. These workers took readings only after exercise (Fig. 10) and the rise in blood pressure to the peak value took place in 40 seconds. In this time they recorded the systolic blood pressure 8 times, a feat that we could not emulate. Their results appear to be incompatible with our findings. It might be thought (as shown in the dotted part of the second curve in Fig. 10) that the fall in blood pressure following exercise and the subsequent rise had been missed in the experiments described in this paper. However, since completing this work, we find that the changes in blood pressure during exercise have been recorded by the oscillographic method with a fine needle inside the brachial artery (Eskildsen *et al.*, 1950), and that the results, using this technique in normal and mildly hypertensive subjects, agreed closely with our own findings. This suggests that the method described in this paper, which had the advantage of simplicity, was also reliable.

In many of the subjects studied under the influence of hexamethonium bromide, the lowering of the blood pressure at rest was due solely to postural hypotension; the suppression of the blood pressure rise during exercise in these cases was as constant as in those in whom the hexamethonium bromide produced a fall in the supine blood pressure. To separate the two hypotensive effects during exercise it would be necessary for the patients to bicycle in the horizontal as well as in the vertical position. This was not done.

We have studied the effect of exercise on the blood pressure and the modification of this effect by hexamethonium bromide in this way, because it is impossible to record continuous blood pressure readings while a person is about his ordinary day's work. It has been shown that the blood pressure can be controlled with hexamethonium bromide during exercise and it is reasonable to suppose that

FIG. 10.—Different patterns of blood pressure response to the exercise test, shown diagrammatically. (A) Response to exercise in normal persons according to Cotton *et al.* (B) The response of normal and mildly hypertensive subjects to the exercise test described in this paper. (C) Pattern of response in intermediate group with hypertension. (D) Pattern of response in severe hypertension. (E) Pattern of response in pre-malignant hypertension. (Z) Moment of relaxation. Potential unfilled venous reservoir. (Z₁) Venous reservoir filled.

an average day's activity will have no ill-effect on the control of the blood pressure by these drugs. This remains true where there is only a postural effect under the influence of hexamethonium bromide.

During the course of this study the existence of different patterns of response of the blood pressure to exercise became evident. These are summarized in Fig. 10. The different patterns of response are clearly related to the severity of the hypertension, but the explanation for this is obscure; it could be related to a damaging effect of the hypertension on the vascular tree or on the heart. The response to an exercise test in hypertension might be used as an ancillary method of assessing the prognosis. We have already some evidence that the type of curve obtained may alter with the worsening or improvement of the hypertension.

SUMMARY

A study has been made of the effect of exercise on the blood pressure of 30 normal and 45 hypertensive subjects. A standard distance of a quarter of a mile has been bicycled on an ergometer. In

the hypertensive subjects, the effect of exercise while under the influence of hexamethonium bromide has also been studied.

All normal subjects showed a rise of systolic blood pressure during exercise of 10–30 mm. Hg.

In mild to moderate hypertension there was usually an increased rise of blood pressure during exercise. The curve of response flattened out as the degree of hypertension became more severe; in the severest cases there was a fall of blood pressure on exertion.

For each patient there was a constant pattern of response of the blood pressure to exercise, providing the clinical state was constant. This pattern remained unchanged under the influence of hexamethonium bromide.

The peak blood pressure on exercise was reduced. In many cases the reduction of the resting blood pressure was purely a postural phenomenon; there was an equally definite hypotensive effect of hexamethonium bromide in these patients on exercise. The postural effect induced by the methonium compounds, far from being an undesirable side-effect, was thus shown to be of major importance in the control of the blood pressure by these drugs.

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