TABLE 3
EXCRETION OF ESTROGEN IN I. U. DURING VARIOUS MONTHS, 1940
(Subject E. M.)

Day of cycle	Jan.	Feb.	Mar.	Apr.
5	50	30	20	...
6	110	120	100	500
10	230	350	380	750
15	40	20	150	100
20	220	75	200	200
24	70	20	120	180
6 day total	720	615	970	> 1,730

elsewhere in the animal kingdom. It is more than ever difficult to state, unless the annual fluctuations are taken into account, what is the normal output of estrogen by a woman.

A more detailed report of this investigation will be published shortly in *Endocrinology*.

HUGH H. DARBY
DOROTHY CHILDS

DEPARTMENT OF BIOCHEMISTRY,
COLUMBIA UNIVERSITY,
NEW YORK

THE EFFECT OF TYROSINASE ON ARTERIAL HYPERTENSION

BECAUSE the substance responsible for some varieties of arterial hypertension may be a simple amine, particularly one containing a phenolic group, a pure preparation of tyrosinase, a phenolic oxidase obtained from mushrooms by Dr. J. M. Nelson, was used in animals exhibiting "renal" hypertension. It was found that tyrosinase is effective in lowering raised arterial pressure in rats and dogs when their kidneys are injured.[1,2] The pressor substance may accordingly contain a phenolic group.

Further evidence for this theory was obtained by ascertaining the effect of tyrosinase upon certain pressor substances. It was found that renin is inactivated by tyrosinase when catechol is present—probably through the mediation of the orthoquinone formed. Angiotonin, obtained from Dr. Irvine H. Page, is also inactivated by tyrosinase when serum is present, suggesting that angiotonin, in its active state, contains a phenolic configuration in the molecule. The pressor substance obtained from the anaerobic autolysate of kidneys, prepared by Dr. Joseph Victor, is inactivated directly by tyrosinase, as is, of course, adrenalin and tyramine.[3]

Since the results in animals were satisfactory, it appeared necessary to ascertain the effect of this enzyme upon hypertension exhibited by human beings. Seventeen patients suffering from arterial hypertension have been treated by daily subcutaneous injections of varying amounts of tyrosinase for three to four weeks. In fourteen the systolic pressure had been persistently above 200 mm Hg and the diastolic above 120. In all but one the blood pressure fell a significant amount; in seven to 140 to 160 mm Hg systolic, and 80 to 100 diastolic, and in six to 160 to 180 systolic and 100 to 115 diastolic. In the other three, the response was less. Three patients in a late stage of the disease were improved. In one there was no effect.

The fall in blood pressure was accompanied by certain other changes, indicating that a general effect upon the disease had occurred. In seven patients whose electro-cardiograms were altered a change in the direction of normal occurred. In three the hearts became small as observed in x-ray photographs. In all but one the level of the urea nitrogen in the blood was lowered, but the clearance of urea was unaffected. Symptoms, when present, were relieved. In four, hemorrhagic and exudative lesions were present in the eyegrounds. These disappeared. No change in the ability of the kidneys to concentrate urine was observed.

When injections of tyrosinase were stopped, the blood pressure soon (within three to six days) returned to its previous level. Symptomatic improvement, as well as the improvement in the ocular fundi, lasted for several weeks or months.

Injections were painful at times; at others no discomfort occurred. Occasionally a moderate degree of pyrexia followed the injections. Allergic reactions at the site of injection developed in three patients.

On one occasion a small amount of enzyme was given intravenously. This was followed by a severe reaction, with nausea, vomiting, signs of increased peristalsis, fall of blood pressure and bradycardia. The blood pressure remained low for twenty-four hours afterward. Significant decrease in the clearance of urea did not occur. Although the blood pressure fell from 220 mm Hg systolic and 150 diastolic to a level of 130 systolic and 90 diastolic for this period, the patient remained comfortable.

Relatively large doses were needed when given by the subcutaneous route. Since the enzyme is a protein, it is doubtful whether absorption was complete. Deposition of grey or yellow pigment at the site of injection was a common occurrence.

It is evident that subcutaneous injections of tyrosinase effectively but only temporarily lower blood pressure in certain cases of arterial hypertension in human beings. These results suggest that some phenolic substance is altered.

HENRY A. SCHROEDER

THE HOSPITAL OF THE ROCKEFELLER
INSTITUTE FOR MEDICAL RESEARCH

[1] H. A. Schroeder, *Proc. Soc. Exp. Biol. and Med.*, 44: 172, June, 1940.
[2] H. A. Schroeder and A. E. Cohn, *Jour. Clin. Inv.*, 19: 769, September, 1940.
[3] H. A. Schroeder and M. H. Adams, "The Effect of Tyrosinase on Experimental Hypertension" (to be published).