Data on 11 Women Taking Oral Contraceptives—*Table continued*

Patient	Age	Diagnosis	Regimen, Dates	Blood Pressure (mm Hg)	Aldosterone Excretion (μg/day)	Urinary Sodium Excretion (mEq/day) Rates	Serum Renin Activity (mμg Angiotensin per ml for 4 hr Incubation)	Serum Renin-Substrate (mμg Angiotensin Generated per ml)	Substrate Reactivity (mμg/ml)	Clinical Information
9	36	Essential hypertension	(Oracon: 12/65 to 4/66)							Hypertension discovered 4/66. Repeatedly normotensive prior to this. Five pregnancies without hypertension. Family history strong for hypertension. BP appears improved since second cessation of treatment.
			4/66	220/115	...	...	...	...	...	
			5/13/66	130/80	...	...	...	...	...	
			6/16/66	160/105	19	178	4.8	945	...	
			(Ovulen 1 mg: 8/12/66 to 11/18/66)							
			9/7/66 (Day 17)	170/95	...	...	4.4	**3,200**	...	
			12/14/66	200/130	...	...	4.9	**1,540**	43	
			1/18/67	150/90	9.1	66	1.7	...	...	
10	30	Essential hypertension	(Ortho-Novum 2 mg; 1/65 to 11/29/65)							Gained 12 lb during therapy. Severe hypertension, headaches, and dizziness. Hypertension disappeared 3 mo after cessation. Remains normotensive 1 yr later.
			11/29/65	180/140	...	...	...	...	...	
			1/20/66	155/100	8.7	143	3.7	...	...	
11	41	Essential hypertension	(Enovid 10 mg daily; 12/10 to 12/29/66)							Essential hypertension of 23-yr duration which began during pregnancy. Transient rise in BP on day 3 of Enovid. No other significant BP changes during 19-day course. Renin-substrate and substrate reactivity markedly increased by third day of therapy.
			10/20/66	...	22	163	1.7	785	30	
			12/12/66	...	21	142	**9.6**	**2,890**	56	
			12/13/66	...	20	41	9.5	**3,840**	53	
			12/14/66	...	...	52	...	**5,135**	53	
			12/16/66	...	30	40	7.7	...	62	
			12/19/66	...	33	52	5.8	**4,650**	56	
			12/29/66	...	26	105	3.3	**3,775**	52	

*Boldface values are outside the normal range.
†SR=secretion rate.

both, introduction of estrogen-progestogen therapy was associated with early rises in serum renin activity and a subsequent tendency to return to normal levels as maintenance therapy continued. This adjustment of the renin activity levels with sustained administration does not always occur, because in patient 6, serum renin activity remained elevated 15 months after starting treatment. The elevated value in this patient and those in the others promptly returned to normal after administration of the medicine was stopped. In none of the patients studied could the observed increases in serum renin activity be attributed to a state of sodium depletion. In all of the patients studied, the range of urinary sodium excretion together with the absence of clinical edema provide evidence for normal sodium metabolism. In two patients (No. 2 and 6), there was a good correlation between observed increases in serum renin activity and increases in aldosterone excretion. However, in five others, the correlation was not apparent. Patients 4, 5, and 11 exhibited increases in renin not accompanied by simultaneously increased aldosterone excretion. Conversely, patients 1 and 8 tended to exhibit disproportionately higher urinary aldosterone values in the presence of relatively normal renin levels.

Comment

It must be appreciated that both the occurrence of hypertensive disease and the use of oral contraceptives are common phenomena in the female, premenopausal adult population. It is therefore important to recognize that the development or enhancement of hypertensive disease in patients taking these medications might be mere coincidence. However, in the present study a specific cause-and-effect relationship is suggested by sequential clinical observations indicating (1) the onset of hypertension in six of the 11 patients after they started taking the medication, (2) the marked improvement or complete correction of hypertension in six out of eight after they stopped taking the medication, and (3) the reappearance and disappearance (for the second time) of hypertension in two subjects who reinstituted medication.

It is of interest that Swaab,[8] in an abstract to the International Congress of Endocrinology, stated that he had observed cases in which blood pressure rose markedly during the use of oral contraceptives. However, to our knowledge, no data have yet been published.

The administration of pharmacological doses of estrogen and progestogen required for contraceptive action was found to produce a number of abnormalities in the renin-angiotensin-aldosterone system, some of which have been previously recognized. Thus, other investigators have also observed significant increases in aldosterone secretion and excretion following administration of Enovid,[9] and