cessfully used against uterine fibromyoma in women(16), possibly due to insufficient quantities of progesterone absorbed(2; p. 167). We feel that it would be of interest to repeat these clinical trials with 19-nor-P instead of P. Absorption from 19-nor-P pellets (pure, not mixed with cholesterol) is probably more rapid than from P pellets.

Summary. Antiestrogenic activities—antifibromatogenic, antihysterotrophic, antiluteinizing—of 19-norprogesterone have been compared to those of progesterone. 19-Norprogesterone, whose progestational activity is considerably greater than that of progesterone, is also strikingly superior as to antifibromatogenic, antihysterotrophic, and antiluteinizing action. On the contrary, the greater progestational potency of Δ^{11}-dehydroprogesterone compared to that of progesterone is seemingly not concomitant with greater antifibromatogenic and antihysterotrophic actions. The theoretical and practical bearings of the statements with 19-norprogesterone are discussed.

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Rauwolfia serpentina in Hypertensive Vascular Disease.*† (21130)

GEORGE A. PERERA.

From the Department of Medicine, Columbia University College of Physicians and Surgeons, and Presbyterian Hospital, New York City.

In recent years, alkaloids of *Rauwolfia serpentina* have been found capable of producing hypotensive and sedative effects and bradycardia in animals and man. *Rauwolfia serpentina* (*Ophioxylon serpentinum*) is a tropical shrub growing throughout the Indian peninsula, the roots of which have been used for centuries for medicinal purposes. The hypotensive properties of the alkaloidal base extracted from this plant have been known since 1931(1), but clinical trials in hypertensive patients in this country were not carried out until a few years ago(2).

The present study was undertaken to throw further light on the clinical, circulatory and metabolic effects of *Rauwolfia serpentina* (Raudixin, Squibb) administered to patients

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TABLE I. Clinical and Laboratory Data of 4 Hypertensive Patients Treated with *Rauwolfia serpentina.*

Patient; Na and K intake, mEq/24 hr	Age, sex	Hosp. day	Dose, mg/d	Avg daily: Wt, kilos	Avg daily: "Resting" B.P., mm/Hg	Avg daily: Heart rate/min.	Avg urine output/24 hr: Vol, ml	Na, mEq	K, mEq
J. DeZ.*	49 ♀	5	0	63.6	150/ 90	76			
Uncomplicated		10–15	0	64.0	140/ 88	77	1520	63	84
Na = 76		16–20	200	64.2	139/ 88	75	1540	60	85
K = 99		21–25	200	64.6	132/ 83	74	1470	59	85
		26–30	200	64.7	130/ 81	72	1540	65	89
		31–34	p†	64.8	133/ 83	74	1720	82	94
P. I.	54 ♂	8	0	71.2	180/110	78			
Cerebral arterio-sclerosis		13–18	0	71.1	162/106	82	1510	77	80
Na = 76		19–23	200	70.8	167/105	80	1610	75	75
K = 91		24–29	200	70.5	160/103	80	1120	60	82
		30–37	300	70.4	156/100	78	1190	84	93
		38–43	300	70.1	157/102	77	1180	62	71
		44–48	p	70.0	158/105	80	1160	72	74
		49–51	p	69.9	157/104	80	1060	67	75
S. R.	35 ♀	3	0	46.3	202/128	96			
Nephrosclerosis		8–13	0	46.8	212/122	85	1670	34	58
Na = 47		14–17	300	47.0	208/124	86	1570	20	54
K = 71		18–21	300	47.5	206/123	84	1530	23	65
		22–25	400	48.0	210/126	80	1960	41	59
		26–29	400	47.8	200/116	80	1930	52	52
		30–33	400	47.5	202/118	80	1880	59	67
		34–37	400	47.0	206/120	80	1530	38	65
		38–40	p	46.8	218/124	80	1610	48	65
		41–43	p	46.4	222/120	86	1330	42	63
D. U.	32 ♀	5	0	56.4	190/120	90			
Nephrosclerosis		10–15	p	56.1	214/128	88	1280	52	66
Na = 58		16–20	300	56.7	200/125	84	1250	30	51
K = 73		21–25	300	56.4	198/120	86	1390	64	64
		26–30	300	56.2	192/116	92	1440	66	67
		31–35	300	—	190/114	80	1120	69	52
		36–38	300	55.5	188/110	80	1510	66	66

* Casual B.P. prior to admission always above 200/120.
† p = placebo.

in various phases of hypertensive vascular disease.

Case material and methods. Clinical observations were made on 10 ambulatory patients with uncomplicated hypertensive vascular disease, and 10 bed patients, on the medical wards of the Presbyterian Hospital, with the accelerated ("malignant") phase of the disorder who showed proteinuria, some degree of nitrogen retention, and retinopathy with papilledema. Four additional patients (one uncomplicated, one with cerebral arteriosclerosis but no cardiac or renal involvement, and 2 with nephrosclerosis but no cerebral or cardiac involvement) were studied in more detail on the metabolic ward. The conditions of study, diagnostic procedures and methods employed in these 4 patients were similar to those reported previously(3), including the utilization of daily "resting" blood pressure measurements, constant dietary and fluid intakes, and preliminary periods of hospital supervision of 2-3 weeks. Known causes of hypertension, such as primary renal or adrenal disease and coarctation of the aorta, were excluded in all instances.

Results. 1. Raudixin, 50-100 mg twice daily, was given orally for one month to the 10 uncomplicated ambulatory patients, casual blood pressures having been recorded at weekly intervals for at least one month prior to therapy. Reductions in arterial tension of more than 15 mm Hg systolic and 10 diastolic (maximum 40 and 28) and in pulse rate of more than 10/min. were achieved in 7 instances within a 2-week period and maintained

throughout the period of drug administration, no significant changes occurring in the remainder. The only side-effect noted was slight nasal congestion in 4 patients. Four of those in whom a response was observed reported that they felt much less tense and nervous. The greatest effects were clearly in those individuals of the tense, hyperkinetic and emotionally labile variety. In no instance did the blood pressure fall to normal and in one patient several retinal hemorrhages appeared for the first time 6 weeks after the start of sustained treatment.

2. In contrast, Raudixin, 100 mg twice daily, administered for periods of 2-4 weeks to the bed patients in the accelerated phase, was without any subjective or objective effects. The casual blood pressure, measured twice daily, averaged 204/126 at the start of therapy and 207/128 at the close. The maximum systolic reduction was 12 mm, and diastolic 8. No significant changes in pulse rate were noted, and no patient showed any improvement in the degree of proteinuria or retinopathy or any decrease in the urea nitrogen concentration in the blood.

3. The results of the more detailed study undertaken in 4 patients are summarized in Table I. This group received Raudixin 100-200 mg twice daily for periods of 15-25 days. Two reported diminished nervousness and emotional tension, and one developed nasal congestion. Both patients with nephrosclerosis showed slight increases in weight during the early part of therapy followed by a decrease. "Resting" blood pressure values, compared to control readings, decreased in all patients to a minor extent, but never more than 10 mm systolic or 10 diastolic below the lowest values recorded in the control period. Changes in heart rate were unimportant and the urine volume fluctuations showed no consistent trends. The 2 subjects with nephrosclerosis exhibited sodium retention for periods of different lengths immediately following Raudixin administration (Fig. 1), subsequent urine sodium values being for a time in excess of the dietary sodium (Table I). The other 2 patients, both receiving a higher sodium content in their diets, reduced their urine sodium content to 39 and 50 mEq on the

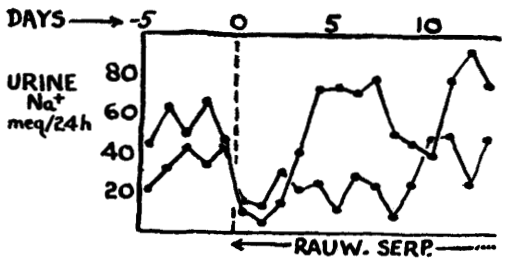

FIG. 1. Effect of Rauwolfia on sodium output in 2 patients with nephrosclerosis.

second day after starting the drug although the mean outputs for 5-day periods were not affected materially. No major alterations in potassium excretion were encountered.

No significant changes were noted in serum sodium, potassium, chloride, carbon dioxide content, urea nitrogen, fasting blood sugar, cholesterol and cholesterol esters, calcium and phosphorus concentrations. The hematocrit, hemogram and urinalysis remained unaltered and the cephalin flocculation test negative. Serial measurements of heart size by X-ray were unmodified, and weekly electrocardiograms and electroencephalograms were unaffected. The plasma volume, measured with the dilution technic employing I^{131}-labelled human serum albumin, increased 300 ml in one subject and decreased 100 ml in another. Under resting conditions, using the direct Fick principle with catheter in right atrium, the cardiac output remained 3.4 l/min. in one patient, rose insignificantly from 3.4 to 3.6 in the second. The splanchnic blood volume was determined in one instance with the change, from 894 to 963 ml, being within the limits of error of the method(4).

Discussion. The present study suggests that Raudixin may modify the casual blood pressure of some ambulatory patients with uncomplicated hypertensive vascular disease. It produces little change in those with the accelerated phase of the disorder or in hospital patients in varying stages of the hypertensive process after an adequate period of bed rest. At least in these short-term observations, rest or the superimposition of the accelerated phase appears to minimize any depressor effect. This observation, together with the absence of any apparent direct cardiac or circulatory action of the drug, lends support to

the concept that only a neurogenic component is modified(5). Whether the depressor action of Raudixin would be of greater benefit if the drug were continued for longer periods, or whether it will modify the natural history of the disease, cannot be stated from the present data. The appearance of retinopathy in one patient while under treatment is noteworthy.

The early and temporary urinary sodium retention, observed in 2 hospital patients with nephrosclerosis, was greater than could be explained by chance fluctuation in subjects on a constant fluid and electrolyte regimen; the transitory decrease in the 2 others may be of no significance. The relationship of *Rauwolfia serpentina* to sodium metabolism or the possibility that it may exert temporary effects on renal function will require further elucidation.

Raudixin seems to be a relatively safe drug and may be of value in the treatment of ambulatory hypertensive patients, particularly those who are tense, hyperkinetic and without complications. Its influence on the course of hypertensive vascular disease remains to be established.

Summary. 1. *Rauwolfia serpentina* (Raudixin Squibb) was administered for periods of 2 weeks or more to 10 ambulatory patients with uncomplicated hypertensive vascular disease, 10 bed patients with the accelerated phase of this disorder, and to 4 hospital patients in varying stages of the disease, the last group being studied in detail while on a constant fluid and dietary regimen. 2. Significant depressor effects and bradycardia were observed in the majority of the ambulatory patients; some degree of relaxation was noted in those who were emotionally tense; but little or no effects were evident in those with the accelerated phase or those under hospital supervision. 3. Temporary sodium retention was apparent in 2 hospital patients with nephrosclerosis, but otherwise Raudixin appeared to have no direct hemodynamic, circulatory or metabolic action.

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Phagocytosis Influenced by Growth Media, Filter Paper and *para*-Hydroxybenzoic Acid. (21131)

EDWIN M. LERNER, II AND JOSEPH VICTOR.

From the Biological Laboratory, Chemical Corps, Camp Detrick, Frederick, Md.

Earlier studies(1) demonstrated greater phagocytosis of *Escherichia coli* grown in beef infusion medium than when grown in tryptose medium. Phagocytosis of killed *E. coli* was increased also by previous treatment with filter paper or *para*-hydroxybenzoic acid(2). The latter compound, an active principle in filter paper, was reported by Davis(3,4) as a new bacterial vitamin and antagonist for *para*-aminobenzoic acid. These observations have been extended to *Brucella abortus*.

Materials and methods. Culture media. *Brucella abortus* strain 19 was kept routinely on Bacto Tryptose agar enriched as noted below, and inoculations were made from 24-hour cultures into the media to be tested. In the initial studies on phagocytosis of *Brucella* grown in beef and tryptose broth, the stock inoculum was carried in tryptose broth and transferred every 24 hours. When daily transfers of the stock culture were made in this broth medium, phagocytosis of both beef and tryptose grown bacteria by neutrophiles from normal guinea pigs under standardized