14554 P

Effect of Veratrone on Urine Volume and Urea Clearance in Hypertensive Toxemias of Pregnancy.

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Although the use of veratrum viride, a combination of alkaloids from the rhizomes of the green hellebore, has for the most part been discontinued, the recent report of Bryant and Fleming[1] suggests that it may have some value as an adjunct to the treatment of eclampsia.

The predominant physiological effect of the drug in animals is central vagus stimulation resulting in a marked fall in pulse rate and blood pressure. Recently an effect on the peripheral vascular system was demonstrated by Willson and Smith.[2] They were able to produce a fall in blood pressure without change in pulse rate when the drug was given to vagotomized dogs. Likewise, an increased perfusion rate through the kidney, the isolated hind leg, and ear of rabbits occurred when the drug was added to the perfusion fluid.

Because information concerning the effects of the drug in the human being is so limited it seems necessary that a complete investigation of the action of veratrum viride on the blood vascular system in the pregnant woman be made. This report concerns the preliminary results of the first of a number of such studies being carried out by us.

Method. The subjects were all prenatal patients confined to the hospital and at complete bed rest. On the morning of the test 200 cc of water were given by mouth every half hour starting at 7:00 A.M. until a total of 1800-2000 cc had been taken and urine specimens were taken by catheter at half hour intervals. The bladder was emptied completely each time. A control urea clearance was started at the end of one hour and the drug, Veratrone, a preparation of veratrum viride for parenteral use, was administered shortly after the completion of the initial test period. Usually at least 2 more clearances were run after the drug had been given; however, in some instances this was impossible because of suppression of urinary output. Only one blood specimen was taken because no appreciable change in the blood constituents was observed. Blood pressures were all taken by one individual with a mercury manometer.

Results. Twelve tests have been run on 10 subjects: 5 pre-eclamptics, 4 hypertensives, and one normal. The study was repeated on the seventh postpartum day on 2 patients.

1. *Effect on Blood Pressure.* A drop in both systolic and diastolic blood pressures followed the administration of veratrone in each instance. The effect was first noted in about 10 minutes and the most pronounced effect on blood pressure occurred about 2-2½ hours after the drug was given. A more marked reaction occurred with larger initial dosages and an increasing effect occurred with subsequent injections.

2. *Effect on Urine Volume.* Associated with the drop in blood pressure was noted a decrease in urine output. This was more marked in the pre-eclamptics than in the hypertensives. One of the former was anuric for 2 hours and another for one hour after a depression of systolic blood pressure from 170 mm Hg. to 100 mm Hg.

3. *Effect on Urea Clearance.* In most instances the urea clearance was decreased when measured during the periods of low blood pressure. The decrease was progressive in the periods studied and in one instance the depression amounted to over four-fifths of the control period.

These changes are illustrated in Fig. 1.

Discussion. The administration of veratrone to patients with the hypertensive tox-

[1] Bryant, R. D., and Fleming, J. G., *J. A. M. A.*, 1940, **115**, 1333.

[2] Willson, J. R., and Smith, R. G., *J. Pharm. and Exp. Therap.*, 1943, **79**, 208.

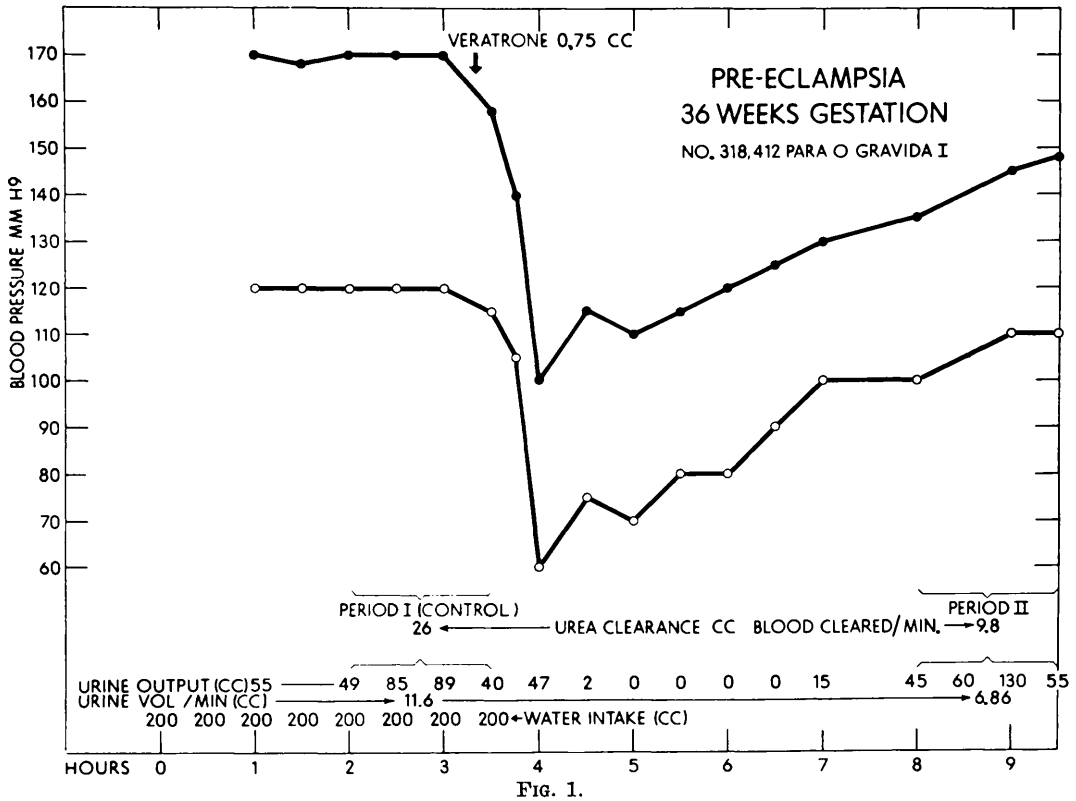

FIG. 1.

emias of pregnancy not only lowers the blood pressure but also decreases kidney function as demonstrated by a depression both in urine volume and urea clearance. It is the opinion of the author that this is the result of two factors: the fall in blood pressure and an alteration in renal dynamics resulting from the action of the drug on the vascular system. Studies on kidney blood flow and glomerular filtration will aid in determining the answer to this problem.

14555

Effect of Xyloquinone in Normal Dogs and Dogs with "Neurogenic Hypertension."

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Some evidence supports the view that hypertension observed in experimental renal ischemia is due to faulty deamination of amino acids.[1,2] By the action of decarboxylases pressor amines are formed in the kidney as intermediary products in the metabolism of certain amino acids. In the kidney with a normal blood supply these amines are deaminized to inert substances through the action of the enzyme, amine oxidase. However, in renal ischemia this latter enzyme is not active and

[1] Holtz, P., and Luedtke, K., *Arch. Exp. Path. u. Pharm.*, 1939, **191**, 87.

[2] Bing, R. J., *Am. J. Physiol.*, 1941, **132**, 497.