

381 CARDIOVASCULAR EFFECTS OF GUANAZOLE (NSC 1895). J.A. Vick, Microbiological Associates, Inc., Bethesda, Md. (Introduced by J. Leiter)

Guanazole, has been shown to exert strong antitumor activity against L1210 tumors in mice. In preclinical studies, guanazole given intravenously has produced a transient flushing at the higher dose levels. Clinically, this response could produce undesirable effects and it is the purpose of this investigation, therefore, to study the mechanism and prevention of the hypotensive action of guanazole. 68 dogs were used to study changes in arterial blood pressure, heart rate, respiration, EKG, EEG and right ventricular pressure. Guanazole produces a sharp drop in arterial pressure, an increase in right ventricular pressure, a slight decrease in heart rate and a rise in central and portal venous pressures. These changes last for from 5 to 10 minutes, and can be partially ameliorated by diphenhydramine, LSD and phenoxybenzamine. Guanazole infused over 25 minutes caused only a rise in right ventricular pressure. The change in right ventricular pressure can be mimicked by injection of 5HT and prevented by LSD. 10 isolated perfused dog hearts and 8 isolated lung preparations were also studied. Guanazole produces a marked increase in left ventricular contractile force and a sharp drop in pump perfusion pressure in the isolated heart. These changes are much like those seen following serotonin and can be prevented by LSD. Guanazole produces a decrease in pulmonary vascular resistance in the isolated lung due to a direct action of the drug on that bed. (Chemotherapy, NCI, NIH Contract PH 43-68-1283).