

Effects of Prolonged Viosterol Administration and of Artificial Sunlight Irradiation on Experimental Tuberculosis in Rabbits.*

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At the 1932 meeting of the National Tuberculosis Association, we reported favorable results from the treatment of tuberculous guinea pigs with viosterol and ascending doses of tuberculin.¹ In the present work a similar though more extensive investigation was performed upon albino rabbits. In addition to the viosterol-treated animals, certain groups were treated with artificial sunlight irradiation to determine whether the irradiation might not have an effect similar to that produced by viosterol.

The rabbits were inoculated subcutaneously with a lethal dose of bovine tubercle bacilli (0.01 mg. of a culture, 0.001 mg. of which was known to produce tuberculosis in the rabbit) and were divided into 6 groups of 8 animals each. The respective groups received treatment as follows: I, viosterol; II, viosterol plus tuberculin; III, ultraviolet irradiation and maize oil; IV, ultraviolet irradiation and maize oil plus tuberculin; V (tuberculin controls), tuberculin and maize oil; VI (untreated controls), maize oil. The amounts of maize oil given to the groups that did not receive viosterol were in every case equal to those given to groups I and II as a medium for the viosterol.

Treatment was started 21 days after the inoculation. The original 10,000 X viosterol solution† was diluted with maize oil to contain 1.46 mg. in 0.05 cc.; this amount per pound of body weight was given weekly by intramuscular injection. Tuberculin (bovine, O.T.) was given subcutaneously simultaneously with the viosterol in weekly ascending doses from 0.00001 mg. to 18.5 mg. for 34 consecutive weeks. Irradiation was given every second day. For the source of light a carbon arc lamp drawing 66 amperes with 48.5 volts across the arc was used. The intensity of radiation of visible

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¹ de Savitsch, E. C., Trevorrow, V. E., Black, W. C., and Lewis, R. C., *Tr. Nat. Tuberc. Assoc.*, 28th annual meeting, 1932, 187; *Am. Rev. Tuberc.*, 1933, **28**, 699.

†Furnished through the courtesy of Mead Johnson and Co.

and ultraviolet light from the arc was equal to 80 watts per square meter at a distance of one meter with 38% of this coming from rays shorter than 4000 Ångstrom units. The initial dose for the irradiation was 2 minutes at a distance of one meter from the arc. This was gradually increased to 12.5 minutes at 0.7 meter on the forty-second treatment; after this, the dose remained constant and was sufficient to cause a definite erythema of the rabbits' ears. In the combined irradiation and tuberculin group, irradiation was given every second day; tuberculin, in weekly doses. At the death of an animal, autopsy findings were recorded and tissues were examined histologically. During the 34th week, the surviving animals were sacrificed.

The results obtained indicate that both prolonged administration of viosterol and irradiation markedly increase the tendency toward central calcification of necrotic tubercles. The incidence of such calcification was most marked (92 to 94%) in the groups that were treated with viosterol alone, with viosterol and tuberculin, and with irradiation and tuberculin, respectively, and somewhat less so (60%) when irradiation without tuberculin was used. These figures are in contrast to an incidence of 25% calcification of tubercles for the tuberculin controls, and of 14% for the untreated controls. However, the degree of organ involvement was greater, and the survival period less, in the animals that received treatment with viosterol or by irradiation than in those of the control groups. When tuberculin was used in conjunction with either of the other treatments, this detrimental effect was definitely less pronounced, but still evident.

The average figures for the survival period of each group are: I (viosterol) 165 days; II (viosterol plus tuberculin) 183 days; III (ultra-violet irradiation and maize oil) 190 days; IV (ultra-violet irradiation and maize oil plus tuberculin) 222 days; V (tuberculin and maize oil) 266 days; VI (maize oil) 258 days.

Our failure to obtain a positive therapeutic effect from the viosterol-tuberculin treatment in rabbits similar to that observed by us¹ in guinea pigs cannot readily be explained, but the beneficial results reported by de Savitsch, Stewart, Hanson, and Walsh² in tuberculous rabbits similarly treated for a shorter period of time suggest that the larger total amount of viosterol used by us may have proved detrimental on account of its toxicity to the rabbit.

² de Savitsch, E. C., Stewart, J. D., Hanson, L., and Walsh, E. N., *Tr. Nat. Tuberc. Assoc.*, 29th Annual Meeting, 1933, 216.