

within about half an hour and returned after two to three hours. The serum cholinesterase activity fell and the readings of the dynamometer rose; these changes occurred at about the same time as the clinical improvement. The injection of di-isopropylfluorophosphonate (0.1–10 mgm.) caused no obvious immediate clinical improvement, but the serum cholinesterase activity fell and the dynamometer readings rose within half an hour, and these changes lasted longer than the corresponding changes after neostigmine.

The absence of clinical improvement in spite of a marked fall in serum cholinesterase in these experiments was interesting but disappointing. It was, however, noticed that dynamometer readings taken at 10 a.m. showed a small rise lasting a number of days after injections of the drug. Experiments were therefore undertaken to test the effect of a daily dose. In three patients, 0.5–2 mgm. was injected once daily for periods up to three months. Neostigmine was also given in the early stages of this treatment. In two cases there was marked clinical improvement after one to two weeks of this treatment, and the daily requirements of neostigmine fell. The dynamometer readings taken 24 hours after the injections showed a marked rise, and the serum cholinesterase was reduced by 86–90 per cent. These patients were eventually discharged from hospital and continued to give themselves 0.5 mgm. per day, and have reported satisfactory progress so far. Atropine was given to counteract the muscarine actions of the di-isopropylfluorophosphonate; but in spite of this, all three patients complained of tightness of the chest, and in one case treatment was abandoned because of this effect.

These results are in general agreement with those of Comroe *et al.*³.

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Effect of Calciferol and of Penicillin on Experimental Tuberculosis of Guinea Pigs

AMONG the many points touched upon in recent literature of tuberculosis are: (1) the favourable results in the treatment of lupus, and possibly other forms of surgical tuberculosis, with calciferol¹⁻³; (2) the conflicting results reported by various workers⁴⁻⁶ as to the effect of penicillin. In the course of an extensive experimental study of the chemotherapy of tuberculosis, we have made observations bearing upon these questions which it is thought are of sufficient interest to report briefly.

500-grm. guinea pigs were infected with 0.001 mgm. of human tubercle bacilli (strain H.418) intramuscularly, and after four weeks, when all pigs were tuberculin positive, various treatments were commenced and continued for ten weeks. Survivors of all treated groups and of untreated controls were killed and assessed for infection by the method of Sher and Kloeck⁷. Individual and average assessments are given in the accompanying table; survival times

were also noted. Streptomycin was taken as an active drug control, but only five animals were killed when this experiment terminated, as previous work had shown that the amount of drug given was enough to suppress the disease during the period of treatment (ten weeks).

Details of drug dosage are as follows:

Penicillin: 500 u. / guinea pig / day subcutaneously in saline given in two doses of 200 and 300 units a.m. and p.m.

Calciferol: 2,000 u. / guinea pig / day in arachis oil given with the food.

Streptomycin: 10,000 u. / guinea pig / day subcutaneously in saline given in two doses of 4,000 and 6,000 units a.m. and p.m.

Group	Deaths	T.B. assessments	Average
Untreated (14)	5/14	71*, 74, 53, 85*, 51 88, 85, 49, 88*, 81* 65, 81,* 84, 85	74.3
Penicillin (11)	8/11	75*, 73*, 71*, 73, 83* 61, 86, 88, 82*, 65* 79*	75.5
Calciferol (12)	5/12	88*, 78*, 69, 98*, 66 68, 76*, 86*, 62, 79 71, 71	76.0
Streptomycin (50)	0/50	5 killed at random 4, 2, 4, 2, 2	2.8

* Asterisk denotes death of animal

It is obvious from the results that there is no difference between the extent of tuberculosis of penicillin-treated, calciferol-treated and control groups.

There was no evidence of toxicity or abnormal calcification in the animal treated with calciferol, nor in a group of normal guinea pigs which received 25,000 units of calciferol a day for ten weeks. These doses roughly correspond to those used in the treatment of lupus vulgaris in man.

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Fibrinolysis in the Animal Organism

It is now known that the action of the fibrinolytic substance produced by certain streptococci is due to its properties as an activator for the transformation of a proenzyme present in blood serum and plasma into a proteolytic enzyme acting on the fibrin. This activation can also be carried out by treatment with chloroform (for references see Christensen¹ and Kaplan²). Considerable confusion concerning the nomenclature for the substances interacting in the fibrinolysis exists; but it seems most logical to use the proposal of Loomis, George and Ryder³. According to this, the name 'fibrinolysin' is used for the active fibrinolytic enzyme, while the inactive pre-