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Inhibitory Effect of Jaundice on the Growth of the Tubercle Bacillus.*

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During the past year we have carried on studies to determine whether whole bile, or any one of its components, exercise growth inhibiting effects on the human, bovine, and avian types of *B. tuberculosis* either *in vitro* or *in vivo*. To determine the former possibility tubercle bacilli were grown on various media containing ox-bile, as well as on glycerine agar containing various percentages of cholesterol and cholic acid, respectively.

The *in vivo* experiments were carried out in guinea pigs and rabbits. While ox-bile, suspensions of cholesterol, as well as of cholic acid were administered intraperitoneally and intravenously, procedures which suggested themselves in part by the observations of earlier investigations.^{1, 2, 3, 4, 5, 6} Furthermore, experimental jaundice was induced in a series of rabbits by ligation of the common bile duct. Some of these animals were then given intravenous injections of virulent tubercle bacilli; others were similarly injected with bacilli grown on cholesterol and cholic acid media. Unjaundiced controls were given corresponding inoculations.

As has already been pointed out by Calmette^{1, 2} tubercle bacilli grow well in the presence of ox-bile, the tendency being to lose their acid fastness if kept transplanted on such media for longer periods of time. Tubercle bacilli grown on glycerine agar mixed with varying quantities of cholesterol, however, do present interesting cultural responses. Good growth is observed on ½ to 1½% cholesterol glycerine agar, there being well defined retardation when 2 to 5% is reached. It is interesting to note that this retardation in growth persisted for about 8 weeks, after which the organisms pro-

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¹ Calmette, A., and Guérin, C., *Compt. rend. Acad. d. sc.*, 1908, **147**, 1456.

² Calmette, A., Tubercle bacillus infection and tuberculosis in man and animals, Eng. tr. Soper, W. B., and Smith, G. H., Baltimore, 1923. Williams and Wilkins, 689 pp.

³ Chamberlain, E. N., *J. Physiol.*, 1928, **66**, 249.

⁴ Grasselle, A., *Arch. di path. clin. Med.*, 1929, **8**, 1.

⁵ Hinze, V., *Z. f. Tuberkheilk.*, 1928, **52**, 199.

⁶ Shope, R. E., *J. Exp. Med.*, 1928, **48**, 321.

ceeded to grow in a relatively normal manner. The reason for this preliminary inhibition with subsequent normal growth is not as yet clear to us. What seemed to be mutation forms similar to some described by Sweany⁷ presented themselves in part of the cultures thus treated. That they were not contaminants seems to have been fully ruled out. These experiments are to be repeated shortly with the sodium salt of cholic acid added in varying percentages to glycerine agar.

In the guinea pigs, attempts to produce jaundice by tying off the common bile duct met with failure, since these animals invariably died of shock by the fifth day. This we found later had already been pointed out by Hewlett.⁸ The injection of whole bile intravenously and intraperitoneally likewise proved futile. Rabbits, however, survived bile duct ligations nicely. Rabbits so jaundiced, and given intravenous injections of bovine tubercle bacilli, survived longer and at autopsy showed less in the way of lesions than the controls. Jaundiced rabbits inoculated with tubercle bacilli grown on varying percentages of cholesterol glycerine agar showed about as extensive lesions as the controls. Forty-five rabbits and 16 guinea pigs were used in these studies.

The studies are being continued, both with reference to the influence of jaundice on experimental *B. tuberculosis* infections and the influence of bile and bile derivatives on cultures in the test tube. A special point will be made to also study the influence of artificially induced hyper-cholesteria in rabbits on the course of experimental tubercle bacillus infections in these animals.

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Relation of Calcium and Phosphorus of Diet to Toxicity of Viosterol.*

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The discrepancies apparent in the literature as to the toxicity of viosterol may be attributed to (1) differences in the potency of the

⁷ Sweany, H. C., *J. Am. Med. Assn.*, 1926, **87**, 1206.

⁸ Hewlett, A. W., *Pathological Physiology of Internal Diseases*. D. Appleton and Company, 1923, 336 pp.

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