

mits us, for the first time, to lay the groundwork for a quantitative method for the titration of thromboplastin. By mixing the unknown material with an excess of purified prothrombin, one can bring about the rapid development of thrombin in the solution. The titer of this thrombin solution is directly proportional to the amount of thromboplastin present. This method is analogous to the one developed and used in this laboratory for the titration of prothrombin.

Summary. Thromboplastin is consumed when it reacts with prothrombin in the presence of calcium ion. This finding eliminates support for the old concept that thromboplastin is a traditional enzyme, capable of converting unlimited quantities of prothrombin into thrombin. Evidence is presented which shows that the quantity of thrombin produced from an excess of prothrombin is directly proportional to the quantity of thromboplastin added to the reaction mixture. When, on the other hand, thromboplastin is present in excess, the amount of thrombin formed is proportional to the amount of prothrombin added.

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Occurrence of the Pellagra-Like Syndrome in Range Chicks.

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In chick virus transmission experiments it is sometimes necessary to use range chicks hatched away from the laboratory. The presence or absence of borderline nervous symptoms are often neither observed nor detected as part of the experimental procedure. The use of commercial rations is usually unsatisfactory in relieving cannibalism,¹ and other findings such as delayed prothrombin clotting values may occur in supposedly normal chicks.^{2, 3}

This note summarizes the results of an investigation of the occurrence of the pellagra-like syndrome in range chicks maintained on an adequate ration.

In over a thousand pullorum-free White Leghorn chicks maintained since hatching (April 12) at a farm range, over 200 presented

¹ Bass, C. C., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **40**, 488.

² Schønheyder, F., *Am. J. Physiol.*, 1938, **123**, 348.

³ Mason, H. C., and Smith, M. E., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **41**, 583.

symptoms of which a laboratory report diagnosed as "*B. coli* bacillosis." Visiting the farm and recognizing pellagra-like symptoms of Ringrose, Norris and Heuser⁴ in varying degrees of severity on eyes, beaks, toes and feathering, present in the 85 survivors at the time (May 20), they were then removed to the laboratory. The chicks had been maintained on the following hatching ration prepared carefully on a commercial scale per 2600 lbs :

Fish meal	130
Milk	200
Meat scraps	100
Soy bean meal	100
Whey	50
Barley	120
Ground oats	400
Bran	400
Corn meal	400
Middlings	400
Dehyd. alf. meal	200
Bone meal	25
CaCO ₃ , MnSO ₄	35
Salt-iodine	25
Cod liver oil XX	15

The diet and water were supplied *ad libitum*. The chicks were permitted to range freely from the shelter.

In the laboratory the chicks were placed on an approved commercial ration fairly satisfactory for chicks but not for adults. Neither cannibalism nor paralysis was observed on crowding. Post-mortem examination of the chicks that died during the first few days in the laboratory revealed gizzard erosions and duodenal inflammation. Food residues were almost absent. The liver showed a deep dirty-yellowish color, while the spleen and kidneys showed small amounts of inflammation. Gas was present in the entire intestinal tract. These findings probably account for the diagnosis of "*B. coli* bacillosis", which was confirmed in the severely affected chicks, and is a common postmortem finding. The sacrifice of several mildly affected chicks did not reveal the bacillosis. The majority of the chicks recovered uneventfully in from 2 to 4 weeks, although the rate of recovery was not uniform, but progressed rapidly for those mildly affected.

The weights and sizes of the chicks were found to be extremely variable and gave no clue as to the defect of metabolism since the majority of the chicks on the ration were observed to be free of the symptoms. However, the chicks that were retarded in growth presented the most severe external lesions at the eyes, mouth, feet, and feathers identical to chicks maintained on the "F" ration of Ringrose, *et al.* The margins of the eyelids were granular, and

⁴ Ringrose, A., Norris, L., and Heuser, G., *Poultry Sci.*, 1930-31, **10**, 166.

firmly stuck together by exudate. No xerophthalmia or cataracts were found. Crusty scales were present at the corners of the mouth. The outer layers of skin on the bottoms of the feet and between the toes were discolored, fissured and peeled wherever cracked. Feathering was markedly retarded and the feathers were dirty, rough and staring with spotty loss.

Substances contained in the vitamin B complex have been shown to be of essential importance for nervous system protection. Shattuck⁵ has pointed out that failure to assimilate and utilize these substances may be as potent a cause of neurologic pathologic changes as is the failure to ingest adequate amounts of vitamin.

Since results with nicotinic acid in chicks and rats have been negative,^{6, 7, 8} it is probable and not at all unlikely that the chick's resistance to pellagra may depend on more than one factor.⁹ The fact that the chicks recovered on the laboratory ration may not mean that the filtrate factor¹⁰ was not lacking, but that the need for it was diminished, although the range ration meat scrap content should have contained sufficient quantity of the factor.

It may be concluded from these observations that the occurrence of the pellagra-like syndrome in these range chicks maintained on a supposedly adequate ration is not significantly different from that observed experimentally in the laboratory and is of great interest bacteriologically, since the *B. coli* bacillosis was not a consistent finding. The significance of these results is to indicate further the lack of relationship between the paralytic factor of Norris¹¹ and Bethke¹² and the growth-promoting factors in the chick. It also points to the existence of borderline deficiency syndromes in range chicks maintained on supposedly adequate rations, and indicates that the factors of nutrition and metabolic disturbance, when the preventive reserve is low, play an important etiologic rôle in similar conditions in other range flocks.*

⁵ Shattuck, G. C., *J. A. M. A.*, 1938, **111**, 1729.

⁶ Cook, C. A., Clarke, M. F., and Light, A. E., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **37**, 514.

⁷ Macrae, R. F., and Edgar, C. E., *Biochem. J.*, 1937, **31**, 2225.

⁸ Emerson, G. A., and Evans, H. M., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **38**, 195.

⁹ Mitchell, H. H., *J. Biol. Chem.*, 1919, **40**, 399.

¹⁰ Lepkovsky, S., Jukes, T. H., and Krause, M. E., *J. Biol. Chem.*, 1936, **115**, 557.

¹¹ Norris, L. C., Heuser, G. F., and Wilgus, H. S., *Poultry Sci.*, 1930, **9**, 133.

¹² Bethke, R. M., Record, P. R., and Kennard, D. C., *Poultry Sci.*, 1931, **10**, 355.

* After this manuscript was ready for publication an article by Mohammad, Emerson, Emerson and Evans on "Multiple Nature of the Rat 'Filtrate Factor'—a Component of Vitamin B₂" appeared in *Science*, October 20, 1939, issue.