

a few instances a concentrate,|| which could be given parenterally when necessary, was tried.

After each of the 3 widely different sources of the vitamin had been tested on 7 dogs under "normal" conditions, the animals were fed a stock diet and morphine administration begun.¶ The initial dose was 10 mg per kilo, which was increased as tolerance permitted, first to 20 mg per kilo, and finally to 30 mg per kilo. When tolerance for this greatest dose was so well developed that the dogs appeared to enjoy "normal" health, the animals were again fed the artificial B₁-deficient diet, the tissues saturated with vitamin B₁ as described above, and the same sources of the vitamin retested for their effects on the anorexia. Finally, wherever possible, following a long period during which the drug had been withdrawn and the animals appeared to have returned to an essentially "normal" state, the tests were repeated. These final trials were not possible in all cases because many dogs died suddenly for reasons not evident on gross examination or at autopsy.

The results yielded no evidence that chronic morphinism *per se* increases the dog's requirement for vitamin B₁.

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Influence of Ingestion of Raw and Desiccated Pancreas Upon Blood Lipids During Infection.*

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It has been shown that there is a definite lowering of the levels for the plasma lipids at height of an acute infection as compared with the values obtained during convalescence.¹ There is, however, a tendency for the lipid content of the blood plasma to rise very

|| Made according to the method of Stuart, E. H., Block, R. J., and Cowgill, G. R., *J. Biol. Chem.*, 1934, **105**, 463, and kindly furnished by Dr. H. W. Rhodhamel.

¶ I wish to thank Dr. Henry G. Barbour of the Laboratory of Pharmacology for supervising the morphinization of these animals.

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¹ McQuarrie, Irvine, and Stoesser, A. V., *PROC. SOC. EXP. BIOL. AND MED.*, 1932, **29**, 1281.

slowly and to remain below the normal range during the period of recovery as long as any infection is still present. This condition of the plasma lipids during an illness in the child has been found to be quite similar to the changes which have been observed by Chaikoff and Kaplan in the blood lipids of depancreatized dogs maintained with insulin.^{2, 3}

The depancreatized dogs developed a moderate decrease in blood fat, a small drop in the plasma phospholipid values, and a marked fall in the total cholesterol due almost entirely to a reduction in ester cholesterol to the point of disappearance from the blood in some of the animals. The free cholesterol content of the blood serum changed very little. When raw pancreas was included in all diets fed after pancreatectomy, a rise instead of a fall in the blood lipids occurred.

Therefore it was thought to be worth while to feed fresh raw whole beef pancreas to children harboring infections with relatively long febrile periods and demonstrating subnormal lipid values during these periods in order to determine if the glandular tissue was capable of favorably influencing the disturbed lipid metabolism so that a return to normal would occur in a short period of time.

Twelve children ranging in age from 6 to 15 years were chosen for this study. Six of the subjects had acute osteomyelitis; one, septic arthritis; 4, acute empyema of the pleural cavity; and one, empyema with peritonitis. Following the first few days of the illness, 6 patients received raw pancreas 3 times daily in addition to the regular mixed diets of the hospital. The amount of pancreas given ranged from 40 g per meal for the smaller child, to 80 g for the larger child. It was continued throughout the period during which the temperature of the children was elevated and the white blood corpuscle count was above normal. A great deal of difficulty was encountered in getting the subjects to retain the raw pancreas, and therefore in the remaining 6 children, desiccated beef pancreas was employed. From 10 to 20 g was given with each meal and it was fairly well tolerated.

All the blood samples obtained before, during and after the period of pancreas feeding were drawn between 12 and 16 hours after a meal. The first sample of blood was collected just before the pancreas feeding was started and subsequent samples were obtained at approximately 2 to 3 week intervals during the period over which the raw pancreas was administered. The final sample of blood was

² Chaikoff, I. L., and Kaplan, A., *J. Biol. Chem.*, 1935, **112**, 155.

³ Kaplan, A., and Chaikoff, I. L., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 606.

drawn 10 to 14 days after the pancreas feeding had been discontinued at the end of the febrile period. Bloor's methods were used to determine the various blood lipids.⁴⁻⁷

The results are summarized in Table I.

The feeding of fresh raw or desiccated beef pancreas appears to have some influence on the blood lipid levels during a rather long period of infection in the child. There was an increase in most of the blood plasma lipids of the children receiving the pancreas in spite of the fact that previous observations⁸ have revealed that infection tends to keep the serum lipids below the normal range for fairly long periods of time. The cholesterol esters experienced a rapid rise from low levels to values within the normal range before the end of the febrile period. The only exception was in case 9 which showed no change in the cholesterol esters. The free cholesterol remained practically at the same level in all cases during the entire period of observation. The phospholipids made a fine recovery which was maintained in the face of existing infection. This is most significant in view of the fact that recent studies⁹ have shown that the phospholipids are inclined to remain at low levels until well into the period of convalescence. The response of the total fatty acids to the feeding of the pancreas was, however, not uniform. In some subjects there was a rather rapid rise to higher levels; in others, very little change took place, and in a few, an actual fall in the total fatty acids occurred.

The apparent favorable influence of the beef pancreas may be due to the presence of pancreatic lipase in the raw product with consequent better absorption of the fat in the child's diet. Furthermore, the suggestion has been made that the favorable response of the blood plasma lipids to the ingestion of whole pancreas may be caused by the fat added to the diet in the fairly large servings of pancreas with each meal. However, the 6 cases which were given the desiccated beef pancreas did not receive any added fat. The latter product had been prepared by drying whole pancreas at about body temperature and extracting the fat with gasoline.[†] These children showed

⁴ Bloor, W. R., *J. Biol. Chem.*, 1916, **24**, 227.

⁵ Bloor, W. R., and Knudgson, Arthur, *J. Biol. Chem.*, 1916, **27**, 107.

⁶ Bloor, W. R., *J. Biol. Chem.*, 1928, **77**, 53.

⁷ Bloor, W. R., *J. Biol. Chem.*, 1929, **82**, 273.

⁸ Stoesser, A. V., and McQuarrie, Irvine, *Am. J. Dis. Chil.*, 1935, **49**, 658.

⁹ Stoesser, Albert V., *Am. J. Dis. Child.*, 1938, **56**, 1215.

[†] Furnished through the courtesy of the Eli Lilly and Company Research Laboratories.

the same changes in the blood lipids as those receiving the raw whole pancreas. The unknown pancreatic blood lipid factor or factors referred to by Chaikoff and Kaplan can, therefore, still be considered the subject of further investigation.

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Calcium Factor in Quantitative Determination of Prothrombin.

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The method developed by the author for the determination of prothrombin has on account of its simplicity won wide clinical interest. Its reliability as an index of the bleeding tendency in jaundice has been repeatedly confirmed. Nevertheless, any test based on the use of biological materials presents well recognized difficulties. In the method as originally described,¹ the thromboplastin was a source of trouble because of its variability in potency, but after the writer² had perfected a method for making a preparation which was stable and had a high and uniform potency, satisfactory results have been obtained. It was, therefore, surprising to learn that Stewart and Pohle³ using the method in its present form on normal bloods found: "that the results were extremely variable." They ascribe their difficulties to the concentration of the calcium chloride solution. In the test a 0.025 M solution is used. Assuming that blood contains 10 mg of calcium, a 0.0075 M solution would be equivalent to the concentration of sodium oxalate present in the plasma. One can see that a definite excess of calcium is employed. It was recognized by the author⁴ that calcium beyond a certain concentration has an inhibitory action on the coagulation time. The reason a 0.025 M solution was chosen was as follows: The prothrombin test is an outgrowth of the method originally developed at the Fifth Avenue Hospital for the determination of the clotting time of recalcified plasma and in this procedure a 0.025 M solution was found most

¹ Quick, A. J., *J. Biol. Chem.*, 1935, **109**, lxxiii.

² Quick, A. J., *J. A. M. A.*, 1938, **110**, 1658.

³ Stewart, J. K., and Pohle, F. J., *Proc. Soc. Exp. Biol. and Med.*, 1938, **39**, 532.

⁴ Quick, A. J., *J. Immunol.*, 1935, **29**, 87.