etioallocholanol-3(β)-17-one in the urine of this patient collected during an 8-day noninjection period.

The isolation of etioallocholanol-3(β)-17-one after the administration of testosterone to the human seems to demonstrate the third of a possible 4 androsterone isomers that may arise by the reduction of the α,β unsaturated ketone ring A of testosterone. The isolation of the other 2 isomers, that is, androsterone and etiocholanol-3(α)-17-one, have been adequately described previously.[1, 2, 3] Only one isomer now remains to be isolated, this one being etiocholanol-3(β)-17-one. Attempts are being made to demonstrate this substance as a metabolite of testosterone.

11991

Cure of Signs of Egg White Disease by Corn Oil Fatty Acids and Vitamin B_6.

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Gyorgy, *et al.*,[1] believe that the various nutritional dermatoses of the rat are clinically quite different. However, there appear to be some similarities between "egg white" dermatitis[2, 3] and the signs of the fat deficiency disease described by Burr and Burr[4] which is due to the absence of certain essential fatty acids from the diet. The influence upon "egg white" disease of corn oil which is rich in one of these—linoleic acid—has been determined. A typical experiment is described. This type of experiment has been repeated twice with larger groups of animals in very nearly the same manner and with identical results.

A diet composed of casein 50, sucrose 20, Osborne and Mendel[5] salt mixture 5, brewer's yeast (Anheuser-Busch strain G) 5, cod liver oil (tested) 5, and Crisco 15 allows normal growth, maintenance and reproduction in the albino rat without any evidence of alopecia or skin pathology. When the casein in this diet is replaced by com-

1 Gyorgy, P., Sullivan, M., and Karsner, H. T., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 313.

2 Boas, M. A., *Biochem. J.*, 1927, **21**, 712.

3 Parsons, H. T., *J. Biol. Chem.*, 1931, **90**, 351.

4 Burr, G. O., and Burr, M. M., *J. Biol. Chem.*, 1929, **82**, 345.

5 Osborne, T. B., and Mendel, L. B., *J. Biol. Chem.*, 1918, **34**, 131.

mercial dried egg white the characteristic dermatitis of "egg white disease"[3] is produced. This egg white diet was fed to Groups C and D (3 female rats in each group) of this study. The diets fed to groups A and B were similar except for the replacement of 10% of the Crisco with a commercial corn oil (Mazola, a corn oil from which some of the saturated fatty acids have been removed) as a source of linoleic acid. The results were very striking. Almost from the start (when the rats were 40 days old) of the feeding of the egg white diets the rats receiving corn oil (Groups A and B) gained weight better (Fig. 1) than the others (Groups C and D). After 60 days upon the diets, egg white acrodynia was well developed in the rats receiving no corn oil (Table I, 100 days old observations) while there were only questionable spectacled eyes in the corn oil groups.

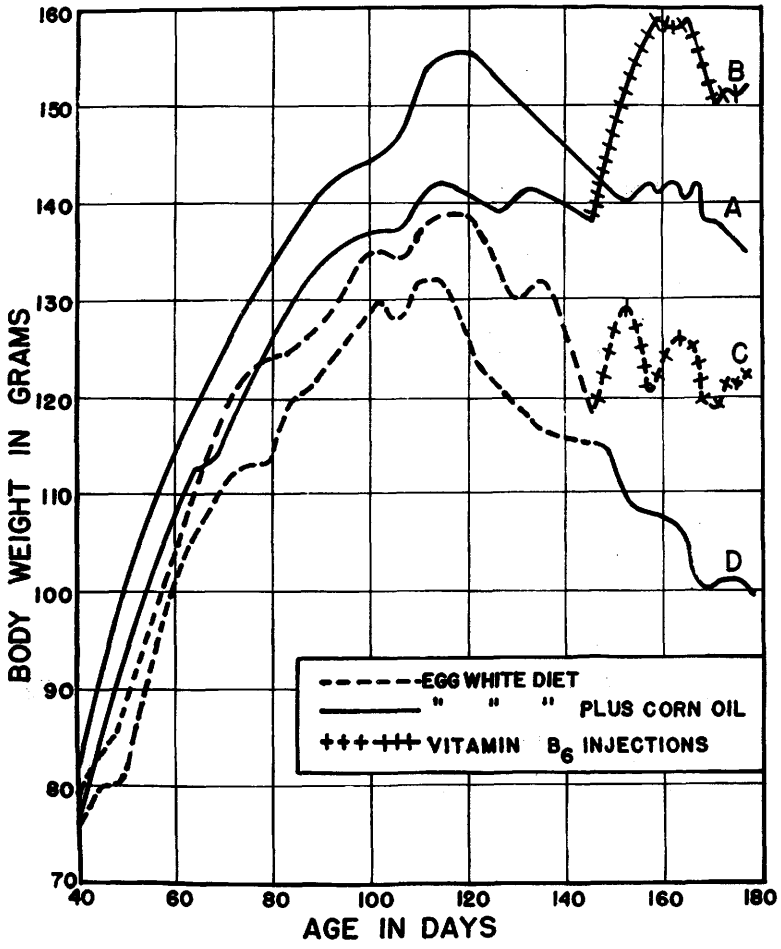

TABLE I.
Influence of Corn Oil and Vitamin B_6 on the Signs of Egg White Acrodynia in the Albino Rat.

Group	Age in days	Treatment		Eyes		Skin		
		Corn oil	Vitamin B_6	Spectacled	Closed	Erythema	Scaliness	Alopecia
A	100	+	0	0	0	0	0	0
B	100	+	0	0	0	0	0	0
C	100	0	0	+	+	++	+	+
D	100	0	0	+	+	++	+	+
A	146	+	0	+	0	+	+	+
B	146	+	0	+	0	+	+	+
C	146	0	0	++	+	+++	+++	+++
D	146	0	0	++	+	+++	+++	+++
A	160	+	0	+	+	++	++	++
B	160	+	+	0	0	0	0	?
C	160	0	+	0	0	++	++	++
D	160	+	0	+	+	++++	+++	+++
A	177	+	0	+	+	++	++	++
B	177	+	+	0	0	0	0	?
C	177	0	+	0	0	+	+	++
D	177	+	0	+	+	+++	+++	+++

At 146 days of age, 106 days after the diet was first administered, the signs of egg white disease were quite marked (Table I) in the groups (C and D) receiving no corn oil and they were losing weight at a rapid rate (Fig. 1). The rats receiving corn oil (Groups A and B) were in much better condition but had lost some hair and there was definite erythema of the belly and forepaws with some scaliness of the skin elsewhere. The sticky secretion which closed the eyes of the rats in the other groups all of the time led to sticking of the lids a fair portion of the time in the rats getting corn oil. In brief, the presence of 10% corn oil in the diet had not prevented the occurrence of the egg white disease but had made it much less severe and the signs of the ailment developed much more slowly than in rats which were not given corn oil.

Birch and Gyorgy[6] suggested a sparing action of linoleic acid on vitamin B_6 which in its own deficiency leads to the development of an acrodynia in the rat. This synergism between vitamin B_6 and linoleic acid has been further described by Birch[7] and Salmon.[8] In order to determine the relation of vitamin B_6 to egg white disease the rats in 2 of our groups (B and C) were each given 0.2 mg daily of vitamin B_6 by subcutaneous injection after they

[6] Birch, T. W., and Gyorgy, P., *Biochem. J.*, 1936, **30**, 304.

[7] Birch, T. W., *J. Biol. Chem.*, 1938, **124**, 775.

[8] Salmon, W. D., *J. Biol. Chem.*, 1940, **133**, lxxxiii.

had been on the special diets 106 days. In Group C, which had no corn oil, this stopped the loss of weight and there was even an evanescent gain in weight. There was a definite improvement in the dermatitis and some of the lost hair was regained. The other group (D), which had not been given corn oil, was changed to the corn oil diet at 146 days of age but the rats continued to fail and lose weight. The very severe dermatitis in this group did not improve and 2 of the 3 rats died just before the experiment was terminated.

Group A, which had been given corn oil in the diet from the start of egg white feeding, continued to lose weight at a slow rate while the condition of the skin became steadily worse and reached a stage (Table I) similar to that reached by the non-corn oil fed rats at a much earlier period. The corn oil fed group (B) which was also given vitamin B_6 showed a remarkable improvement in their condition. They gained weight rapidly and in 14 days had lost all evidence of acrodynia which they had begun to exhibit earlier. The lost hair was rapidly replaced and a questionable alopecia is indicated for this group at the end of the experiment only because the hair growth was not quite as thick as with rats of the same age raised entirely on the stock diet. The injection of vitamin B_6 cured all of those signs of egg white disease which were not prevented by the inclusion of corn oil in the diet.

Discussion. A constituent of various foodstuffs which will overcome egg white injury has long been recognized.[2, 9, 10] Gyorgy and coworkers[11, 12] refer to this factor as vitamin H and du Vigneaud, *et al.*,[13] have shown the identity of Gyorgy's vitamin H with biotin. Our experiments raise the possibility that corn oil and vitamin B_6 may replace or enhance biotin activity. Schneider, *et al.*,[14] find that non-egg white acrodynia may be cured by either the "essential fatty acids" alone or vitamin B_6 plus an accessory factor. If this factor was biotin our results might be explained on this basis. The question of nutritional dermatoses is without doubt a complex one but an adequate supply of linoleic acid in the diet would appear to be desirable in studying any type of acrodynia.

Summary. Egg white injury or acrodynia in the albino rat, which occurs when commercial dried egg white is included in the diet of

9 Lease, J. G., and Parsons, H. T., *Biochem. J.*, 1934, **28**, 2109.

10 Gyorgy, P., *J. Biol. Chem.*, 1939, **131**, 733.

11 Gyorgy, P., Kuhn, R., and Lederer, E., *J. Biol. Chem.*, 1939, **131**, 745.

12 Birch, T. W., and Gyorgy, P., *J. Biol. Chem.*, 1939, **131**, 761.

13 du Vigneaud, V., Melville, D. B., Gyorgy, P., and Rose, C. S., *Science*, 1940, **92**, 62.

14 Schneider, H., Steenbock, H., and Platz, B. R., *J. Biol. Chem.*, 1940, **132**, 539.

this animal in a substantial amount develops much more slowly if 10% of the fat in the diet is in the form of corn oil instead of Crisco. If vitamin B_6 is injected into corn oil fed rats the signs and symptoms of the egg white acrodynia almost entirely disappear.

11992

Studies on Identity of Prothrombin.

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Since Schmidt's[1] work in 1872, there have been many attempts to isolate and identify thrombin and its precursor, prothrombin. Chief among these have been those of Howell,[2] Eagle,[3] Mellanby,[4, 5] Seegers,[6] and Astrup and Darling.[7] Most of these workers have believed that prothrombin is a globulin. Mellanby, Seegers, and Astrup and Darling have probably isolated thrombin in its purest form, and Mellanby has investigated its chemical composition as well as its physiological properties. More recently, Astrup, *et al.*, have, on the basis of precipitation studies with ammonium sulphate, demonstrated that the precipitation pattern of thrombin was that of albumin.

In the course of plasma protein studies in multiple sclerosis,[8] using Butler's[9] method of phosphate buffer precipitation and the Tiselius electrophoresis technic, opportunity was presented to obtain additional data on the identity of prothrombin. Our aim was to show with what fraction of plasma proteins prothrombin precipitated, and how it migrated when subjected to electrophoresis by Tiselius's technic

Oxalated human blood plasma was mixed with Butler's phosphate

1 Schmidt, Alexander, *Pfluger's Arch.*, 1872, **6**, 445.

2 Howell, William H., *Am. J. Physiol.*, 1914, **35**, 474.

3 Eagle, Harry, *J. Gen. Physiol.*, 1935, **18**, 531.

4 Mellanby, J., *Proc. Roy. Soc.*, London, Ser. B, 1931, **107**, 271.

5 *Ibid.*, 1933, **113**, 93.

6 Seegers, W. H., Smith, H. P., Warner, E. D., Brinkhous, K. M., *J. Biol. Chem.*, 1938, **123**, 751.

7 Astrup, Tage, and Darling, Sven, *J. Biol. Chem.*, 1940, **133**, 761.

8 Putnam, Tracy J., to be published.

9 Butler, Allan M., and Montgomery, Hugh, *J. Biol. Chem.*, 1932, **99**, 173.