Experiments by Parsons, Smith, Moise, and Mendel (1930), on the physiological effects of various protein-rich diets showed that cooked, dried, commercial egg white is unsatisfactory for reproduction and lactation when fed to adult female rats as either 80 or 20 per cent of a well supplemented diet. Bond (1922) found that reproduction was not optimum with 30 per cent of egg white in the ration, and Mitchell (1925), using egg white to furnish 18 per cent or more of protein in the diet, came to the same conclusion. That the fault, at least on the highest percentages, does not lie in an inadequacy of the proteins of egg white was indicated by the success of Osborne and Mendel (1913, 1913–14), Bateman (1916), Bond (1922), Mitchell (1925), Cowgill (1927), and Hartwell (1928) in inducing satisfactory growth of young rats with the use of egg white, at relatively low levels, as the sole source of protein in the diet.

Chick and Roscoe (1929), in testing the possible value of egg white as the source of protein in the basal diet for the assay of vitamin B (B₁), found, however, that egg white fed as 20 per cent of a relatively purified diet did not maintain the growth of rats to maturity, the growth of some of the rats becoming subnormal even in the first few weeks after weaning. They suggested that some third factor, not identical with the antineuritic nor the antidermatitis factor, present in yeast, is absent from egg white.

Although Boas (1924) concluded that egg white does not contain protein adequate for complete nutrition, she reported in 1927, after further investigation, that egg white, coagulated before drying and properly supplemented with known dietary essentials supports satisfactory growth and nutrition in young rats, but that dried fresh egg white or commercial dried Chinese egg
white is unsuitable even after cooking for use as the sole protein of the diet of young rats in a similarly constituted ration. Failure in growth, dermal and nervous symptoms, and death of the rats resulted unless one of certain other food substances was included in the diet with the coagulated egg white which had been first dried before cooking. Boas (1927) suggested two alternative possibilities: the development of some toxic substance during the drying of the egg white, capable of neutralization by certain protective foods; or the destruction of some hitherto unrecognized dietary essential when drying the egg white before coagulation. However, neither hypothesis seemed entirely satisfactory.

Norris and Ringrose (1930) have reported a pellagrous-like syndrome in chicks occurring on a diet containing powdered egg albumin. The manifestations of the disease included sticky eyelids, dermal symptoms, and abnormalities of the mouth, stomach, liver, and kidneys.

Experimental Procedure

**Animals**—Albino and hooded rats were used as the experimental animals. The same technique was employed in their care and handling as that described by Parsons, Smith, Moise, and Mendel (1930).

**Rations and Their Preparation**—Inasmuch as the modifications of Sherman’s and of Steenbock’s stock rations used previously in experiments on protein-rich diets (Parsons, Smith, Moise, and Mendel, 1930; Parsons, 1930) had proved inadequate for reproduction in successive generations of rats, 5 per cent of butter fat was added to each of these rations, and a further modification of the Steenbock ration devised by House, Nelson, and Haber (1929), in which 2 per cent of yeast and 10 per cent of wheat embryo are included, was used also. No differences could be detected in the performance of the young rats in respect to these stock rations, when placed on the egg white diets, and hence they are not designated individually in the results.

Certain of the young rats used in the experiments were produced on the following high protein rations: liver 60 per cent, corn-starch 6 per cent, dried yeast 20 per cent, wheat embryo 10 per cent, salt mixture (Osborne and Mendel, 1919) 4 per cent; casein 64 per cent, corn-starch 2 per cent, dried yeast 20 per cent, wheat embryo 10 per cent, salt mixture 4 per cent; beef powder 66 per cent, dried yeast 20 per cent, wheat embryo 10 per cent, salt mixture 4 per cent. Liver was also added in varying percentages to the stock rations of certain of the young before weaning. The egg white rations fed are recorded in Table I.
The egg white employed included both a commercial, dried, Chinese product and egg white from fresh eggs obtained from the University of Wisconsin, Department of Poultry Husbandry. In most of the rations the egg white was fed in a dry powdered form, but for certain of the cooked rations it was not dried.

The commercial dried yeast was assayed for vitamins B and G and found to be potent. The wheat embryo was obtained from a milling company. The liver was prepared by steaming fresh beef liver until it was thoroughly cooked, chopping with a food chopper, drying at room temperature before a fan, and pulverizing.

The egg white was cooked in various ways.

**TABLE I**

*Composition of Rations*

<table>
<thead>
<tr>
<th>Ration</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
<th>F</th>
<th>G</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egg white (dry basis)</td>
<td>66</td>
<td>66</td>
<td>20</td>
<td>20</td>
<td>20</td>
<td>66</td>
<td>66</td>
</tr>
<tr>
<td>Dried yeast</td>
<td>20</td>
<td>10</td>
<td>20</td>
<td>20</td>
<td>0</td>
<td>10</td>
<td>15</td>
</tr>
<tr>
<td>Wheat embryo</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Sugar</td>
<td>0</td>
<td>10</td>
<td>26</td>
<td>46</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Salt mixture*</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Liver (dried beef, cooked)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>20</td>
<td>10</td>
<td>5</td>
</tr>
</tbody>
</table>

* 3 to 5 drops of cod liver oil daily were fed separately.
* Osborne and Mendel (1919).

**Boiled Egg White**—Dry, commercial, raw egg white was softened in cold water and poured into boiling water to which 3.25 cc. of glacial acetic acid for each 100 gm. of dry egg white were added to bring the solution to pH approximately 4.8, the isoelectric point of egg albumin. Inasmuch as these additions checked the boiling, the mixture was again brought rapidly to the boiling point and boiled for approximately 1 minute.

**Cooked for 20 Minutes**—Dried egg white was softened in water and was brought to a temperature of 70° in a double boiler without addition of acid, and was then placed in a drying oven for 20 minutes where it reached a temperature of 80°.

**Cooked for 3 Hours**—Dried egg white was softened in water and was brought to a temperature of 70° in a double boiler without...
addition of acid, and was then placed in a drying oven for 3 hours where it maintained a temperature of 80°.

Methods
For water balance studies, the individual cages inclosed in cylinders of sheet tin were set on top of large glass funnels and the urine collected under paraffin oil in large test-tubes. Water and urine were measured at the end of either a 24 or 48 hour period. The intake of water was determined by refilling the drinking bottle to its narrow mouth from a glass cylinder, thus measuring the amount which had been consumed.

The test for occult blood in urine was made by placing some crystals of benzidine hydrochloride with a few drops of urine on a porcelain plate, and adding a small amount of glacial acetic acid and hydrogen peroxide. A strong blue color develops with even traces of blood.

Results
Among the diets rich in protein which have been tested by the author, that high in egg white is the only one exhibiting markedly unfavorably physiological effects on the rat, in striking contrast with the results obtained with casein, dried liver (Parsons, Smith, Moise, and Mendel, 1930), beef powder,¹ and egg yolk.¹ The unfavorable response to egg white was most striking. Healthy young rats from the stock colony rarely survived more than a few days feeding on egg white Ration A. The symptoms noted were loss of weight, lessened activity, an awkward gait in walking, a humped back, meteorism, increased shedding of hair, soiled fur, paws, and tail, closed eyelids, and bloody urine. The rats were often found dead with the jaws firmly closed on the wire mesh of the floor of the cage, or in other attitudes suggesting extreme spasticity. On autopsy the bladder was frequently found to be filled with bloody urine or drops of dried blood were found on the paper under the floor of the cage. The cecum and sometimes the small intestines and stomach were filled with a greenish black, foul smelling mass. If the animal was not autopsied immediately after death, the abdominal organs and peritoneum often showed a

¹ Unpublished data.
distinct discoloration of greenish black. Diarrhea was seldom noticed on any of the egg white rations but it occurred occasionally on the moist rations. Boas (1927), using a lower percentage of egg white, in her extensive experiments on egg white injury, makes no mention of these initial effects during the first weeks on the diet.

### Table II

**Relative Protection from Egg White Injury during Early Weeks on Ration A (High in Raw Commercial Egg White) Afforded to Rats by Previous Diet**

<table>
<thead>
<tr>
<th>Group</th>
<th>No. in subgroup</th>
<th>Percentage in subgroup</th>
<th>Distribution of rats in reference to initial weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>20-30 gm.</td>
</tr>
<tr>
<td>51 rats produced on stock rations</td>
<td>Surviving</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Dying</td>
<td>46</td>
<td>90</td>
</tr>
<tr>
<td>73 rats produced on rations containing liver</td>
<td>Surviving</td>
<td>68</td>
<td>93</td>
</tr>
<tr>
<td></td>
<td>Dying</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>14 rats produced on high beef powder ration</td>
<td>Surviving</td>
<td>6</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>Dying</td>
<td>8</td>
<td>57</td>
</tr>
<tr>
<td>24 rats produced on high casein ration</td>
<td>Surviving</td>
<td>8</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>Dying</td>
<td>16†</td>
<td>67</td>
</tr>
</tbody>
</table>

* In some added experiments performed by Fern Stone and Marie Stephens, students in the Department of Home Economics, with slight modifications of Ration A, four rats out of forty-seven, raised on stock rations, survived the initial injury, while forty rats out of forty-seven, produced on high protein rations, survived.

† The ration of nine of these rats contained 56 per cent of egg white and 20 of wheat embryo instead of the 66 and 10 per cent, respectively, in Ration A.

In the course of some studies on various high protein diets during reproduction, a number of young rats were weaned on these rations. Groups of these young placed on egg white Ration A showed a strikingly lower rate of mortality than did those from stock rations. Some of the former rats showed practically none
Physiological Effects of Egg White

of the loss of weight and other characteristic signs of the disorder, and other rats recovered quickly. Liver seemed to be the most effective in protection. Casein and beef powder less so. The protective capacity of liver was further tested by feeding it to stock mothers and their young from the birth of the young to weaning and for various fractions of this time. The amount of liver varied from 66 per cent to 5 per cent.

In Tables II and III, the influence of these preliminary diets on the performance of young rats when placed on raw egg white Ration A is apparent. Whereas approximately 90 per cent of the rats from stock rations died after a short interval on Ration A, over 90 per cent of the rats survived which had received prelimi-

TABLE III
Extent to Which Decline of Rats Dying on Ration A (High in Raw Commercial Egg White) is Modified by Previous Diet

<table>
<thead>
<tr>
<th>Rats produced on</th>
<th>No in group</th>
<th>Age when started</th>
<th>Initial weight, average</th>
<th>Maximum weight, average</th>
<th>Minimum weight, average</th>
<th>Days rats lived on average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stock rations ....................</td>
<td>46</td>
<td>23</td>
<td>43</td>
<td>42</td>
<td>33</td>
<td>11</td>
</tr>
<tr>
<td>Rations containing liver ..........</td>
<td>5</td>
<td>19</td>
<td>35</td>
<td>58</td>
<td>30</td>
<td>38</td>
</tr>
<tr>
<td>High beef powder rations .........</td>
<td>8</td>
<td>21</td>
<td>30</td>
<td>40</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>High casein rations ..............</td>
<td>16</td>
<td>26</td>
<td>32</td>
<td>42</td>
<td>30</td>
<td>17</td>
</tr>
</tbody>
</table>

nary feedings of liver. In all of the groups, an influence of the body weight of the rat when started on the egg white ration can be seen, the smaller rats tending to die in greater numbers. Among the rats produced on stock rations, however, some individuals died even though the initial body weight was 60 or even 100 gm. This was not true of those produced on high protein diets or fed varying amounts of liver. Some degree of influence of the previous diet is seen even among the groups which died on egg white (see Table III). The forty-six rats from stock rations, which failed to survive, died on an average after 11 days of feeding, with practically no gains in weight; the five from liver rations died after 38 days, with substantial gains in body weight before the final de-
cline. Their failure to survive seems to have been influenced by the early age at which they were placed on the experimental ration in an attempt to keep the initial weight comparable with other groups of slower growth. Of three litters fed as little as 5 per cent of dried liver from the 18th to the 21st day all except one rat survived on egg white Ration B, losing weight the 1st day on the ration but fully regaining it on the 2nd. However, the growth curves of this group showed a temporary plateau after a week or so of good growth, not typical of the curves of the rats which received a more liberal supply of liver before weaning, suggesting that the supply of a protective factor had become exhausted. The one death in the group occurred at the time of this plateau.

In view of these results it was not surprising to find that the incorporation of from 5 to 20 per cent of liver in the egg white ration itself, for 1 or 2 weeks at the beginning of the experiment, afforded approximately the same protection from the immediate symptoms of egg white injury as that to be derived from a preliminary period of liver feeding. 1 per cent of liver included in the egg white ration for 1 week appeared to be on the border-line of efficient protection.

The question arose as to whether this initial injury depended upon some quality of raw Chinese egg white not possessed by fresh eggs or by cooked eggs. Accordingly eggs were procured, the freshness of which was assured, from the Department of Poultry Husbandry, and the dried white from these was fed as Ration A. Only one rat of a litter of six with body weights of 34 to 36 gm., produced on a stock ration, survived more than 12 days of feeding this fresh dry egg white ration. Fresh egg white was then cooked in the various ways described under "Rations," dried, incorporated with the other ingredients of Ration A and fed to a group of twelve rats with an average body weight of 34 gm. All twelve died within a short time. Chinese egg white acidified and cooked at the boiling point was fed moist, as Ration A, to a group of six rats with average body weight of 80 gm. Four of the six died in an average of 15 days. Obviously the injurious effect of egg white is present when either raw or cooked, fresh or commercial egg white is fed in high concentrations.

Cox, Smythe, and Fishback (1929) have pointed out that the injury which Hartwell (1928) reported in young rats fed rations
Physiological Effects of Egg White

containing 20 per cent of edestin and low in the vitamin B complex, is strikingly similar to that observed by themselves in rats on cystine-rich diets. The performance of young rats on egg white Ration A in the present experiment is also closely comparable. Both Hartwell and Cox, Smythe, and Fishback found that yeast concentrates were protective against injury. Knott observed that previous liver feeding gave a certain degree of protection to young rats on rations containing 5 and 10 per cent of cystine, but that this protection was less effective than in the case of egg white injury.

The question arose as to whether the injury from egg white might not be due to the high yield of hydrogen sulfide. In Ration A fed to two groups of rats the iron content was varied. In the ration of one group the iron citrate was left out of the salt mixture. In the other, 5 times the concentration of iron citrate in Osborne and Mendel's salt mixture was included, with the idea that this might be effective in reacting with the hydrogen sulfide in the digestive tract. There was no difference in the two groups in regard to the severity of the injury or the occurrence of death.

The previous discussion of survival and protection on egg white has referred only to the initial response of the animals to the ration. The surviving rats which either do not suffer even a temporary decline, or which recover on the egg white diet, usually show, during a later period, striking evidence of nutritional disaster unless complete protection has been secured, as for instance by including 20 per cent of dried liver in the egg white ration (Ration E). The first of these signs of nutritional disorder in the second period is usually a fuzzy, woolly appearance of the coat due to the absence of long hairs. At about the same time, the mouth becomes involved. The first indication of this is either scaly, furrowed red patches at the corners of the mouth, or a bare, sharply demarcated area on the lower lip in the shape of either a sharp wedge or a narrow strip. The whole lower lip becomes bare shortly, the color progressing from a pink to a red and assuming eventually an intense angry hue. The upper lip is slower in showing a change, but the final appearance is the same. Swelling is progres-

\[\text{Unpublished data from a thesis presented by Elizabeth Knott in partial fulfilment of the requirements for the degree of Master of Science, University of Wisconsin, 1930.}\]
sive, the lips are distended and have a shiny surface. The bald inflamed areas may spread to the nose, becoming very extensive. No lesions have been observed on the tongue although a cheesy material has been noticed at the base of the lower incisors.

Before the soreness of the lips has progressed far the eyes tend to look watery, and exudate dries on the lids, forming a crust or causing the lids to adhere. When the lids are not closed entirely, the eyeballs appear sunken and glazed, but there is no suppuration as in vitamin A deficiency. There is also almost never an appearance of blood, although the rat scratches and rubs the eyes vigorously enough to produce bald areas around them as in cases of xerophthalmia due to vitamin A deficiency.

While these symptoms are developing, the coat looks more and more unkempt, the hair mats, separates into ribbed bands on the abdomen, and thin or bald areas develop. The period at which baldness occurs, the regions of the body first affected, and the character of the loss of hair vary greatly among individuals, but members of a litter, or litters produced at one time, tend to resemble each other in this respect. At one time, baldness of the back of the head is the most noticeable feature, but at others xerophthalmia may appear first most frequently on the thorax, the scrotum, the back, or other regions. The areas are usually symmetrical but may be small and irregularly scattered. The first extensive loss of hair may be at a period of desquamation when large tufts of hair are shed, attached to the dead skin.

Dermatitis sometimes appears early or may be later in developing. The first change noted is in the color of the skin. On parting the hair on the back of a normal young rat, the skin shows a distinct lavender color. In the animals fed egg white, this shifts to a pink or red; or the first alteration noted may be a dirty whitish appearance due to fine scales. Large crusts form on the back, occasionally on the abdomen, thighs, arms, scrotum, or other parts of the body. On healing, these areas become entirely denuded, leaving a delicate new skin, glistening and light pink in color. After a few days a soft fine coating of hair appears on the denuded areas, including the lips, and growth of this proceeds rapidly and the rat soon resumes a normal appearance. The hair on the back, however, although long, remains coarse as the area lacks the fine undergrowth of normal hair.
The ears have never been observed to be affected. The paws and tail however are more or less involved. In some groups of rats, the hair on the backs of the paws, especially the hind paws, becomes matted, and a fine scale appears. In a number of animals the tail becomes scaly also, especially for an inch or 2 inches at the end. Distinct constrictions and ridges may also appear, and the end of the tail may become gangrenous and drop off. These symptoms were often obscured by a coating of the sticky egg white ration on the tail and paws, and so may have occurred in a greater number of instances than was recorded. In most of the severe cases the wrists become greatly inflamed and somewhat swollen, presumably from the vigorous rubbing of the eyes, mouth, and nose. However, the inflammation usually spreads beyond the surfaces subjected to rubbing, and the entire forearm and paws often become inflamed, swollen, and crusted with scales. As the body becomes emaciated, the skin assumes a characteristic ridged and folded appearance (see Fig. 1).

One striking feature of the dermatitis occurring in almost all of the cases, but which the author has not seen described before for the rat, is a deep pigmentation of the epidermis. Both Sherman
and Sandels (1929) and Goldberger and Lillie (1926) have noted yellow incrustation in pellagrous rats, and Salmon, Hayes, and Guerrant (1928), light brown eschars, but the pigmentation in the present experiment is very dark in shade, tending to a deep brown. It has been noted to occur only on the back, and is bilateral, sharply demarcated, and is usually extensive in area. It is the most persistent symptom at the time of recovery. During the extensive desquamation and formation of new skin of healing it temporarily disappears but soon forms again on the new skin and is only gradually lost, although the rat may appear normal in every other way.

The amount of urine excreted is definitely diagnostic of the advance of the nutritive disorder. With few exceptions, rats severely affected excrete only from 5 to 8 cc. of urine per day, although they may have previously excreted 20 to 30 cc. daily. This is associated with a low water intake and a dehydrated condition of the body, but as the urine excretion is a more constant factor than the water consumed it seems possible that it may be related to the condition of the kidneys. The urine is deep yellow tan, or green in color, but inasmuch as it is concentrated, it is uncertain whether or not it contains more than a usual amount of pigment. When a cure is instituted an increase in water intake and urine volume is among the first changes noted. Inasmuch as the body weight may increase 7 or more gm. per day at first, a retention of water in the tissues doubtless accounts for this increase to a great extent. With only one exception, obviously bloody urine or occult blood in the urine has not been observed in these rats in advanced stages of the disorder, although as noted before, when the rats die within a short time after being started on the diet, bloody urine is frequently observed.

The rats may continue to grow while a part or all of the symptoms so far described are becoming established, but growth ceases when the rat weighs from 75 to 120 or more gm. and for a period of time the body weight remains practically stationary. During this plateau or when the body weight begins to decline, a very definite nervous disorder usually makes its appearance. The rat is observed to sit in a humped, kangaroo-like position. At first this hump flattens out as the animal walks, but later the hump in the back persists as the rat moves about. Priapism sometimes begins
Physiological Effects of Egg White

at an early stage, or may appear later. A progressive spasticity occurs in the legs, particularly the hind legs, first noticeable in the position assumed in climbing the sides of the cage, in which the body is not held close to the cage as in the case of a normal animal, but is held stiffly with the legs extended. The awkwardness in walking then becomes more and more apparent. Finally, sharp jerking motions appear in one or more of the legs as the animal walks. Death is preceded by a rapid loss of weight.

In order to ascertain whether or not the concentration of egg white in the diet bears a relationship to the severity of the nutritional disorder, three litters of six rats each were first protected against initial injury by incorporating 5 per cent of dried beef liver in the stock ration of the mother rats at the birth of the litters, and later when these young reached a body weight of from 40 to 47 gm. they were divided into three groups and fed Rations A, C, and D containing 66, 40, and 20 per cent of egg white respectively. Inasmuch as Boas (1927) found a variety of food substances, including potato starch, to be protective when incorporated into an egg white ration, starch was avoided in these rations and commercial sucrose was used instead in replacing an equal weight of egg white in the mixtures containing the lower percentages of protein, since this carbohydrate has been used successfully by Burr and Burr (1929) and McAmis, Anderson, and Mendel (1929) in highly purified basal rations. At the end of 24 days on the egg white rations, the growth of the rats was found to be inversely gradated to the percentage of egg white in the rations. For the first 24 days, the rats on Ration A made an average gain of 42 gm.; on Ration C, 77 gm.; on Ration D, 102 gm. Five out of six rats on Ration A showed bareness of the lips, and only one out of six in each of the other groups. The experiment was abandoned at this point because a new lot of dried egg white was proving to have a different effect on all of the rats on experiments, leading to prompt cures in the cases of even those which showed the most pronounced symptoms. A difference in the quality of separate lots of egg white was also the experience of Boas (1927) who attributed the better quality of some samples to partial coagulation during drying at high temperatures. The presence of traces of egg yolk in the dried egg white suggests itself also.
The tail and skin lesions noted by Burr and Burr (1929, 1930) on diets low in certain unsaturated fatty acids seemed so nearly identical with those in the present experiments with egg white (see Fig. 2) that the question arose as to whether the origin of the lesions in the latter case might not be a relative deficiency of those fatty acids, although the daily dose of the 3 to 5 drops of cod liver oil in addition to the 10 per cent of wheat embryo in the ration would presumably furnish the minimum amount necessary. In certain experiments, therefore, lard3 from oily hogs (Ellis and Isbell, 1926) and linseed oil, both of which substances are relatively rich in linoleic acid, an essential fatty acid according to Burr and Burr. (1930), were fed. Neither raw linseed oil in amounts as high as 30 drops a day nor 10 per cent of lard in the diet delayed the onset of dermal symptoms. 10 drops daily of both linseed oil and commercial lard proved ineffective in cures also.

With both 5 and 10 per cent of liver in the ration (Rations F and G) moderately severe dermal symptoms occurred although they

3A small sample of "oily" lard was kindly furnished by W. E. Anderson of the Department of Physiological Chemistry of Yale University.
Physiological Effects of Egg White

appeared to be somewhat delayed. In one case on Ration G even the nerve symptoms, associated with late stages of the disorder, were observed. With 20 per cent of liver (Ration E), on the other hand, growth was rapid and the skin and hair retained their normal healthy appearance. It is evident that the protective level of liver in rations high in raw commercial egg white lies between 10 and 20 per cent of the ration. No extent of liver feeding previous to weaning seemed to insure entire protection from the later symptoms of injury in spite of the fact that so small an amount has been shown to protect from the initial injury.

Although by far the greater number of the rats which survived the first phase of the egg white feeding on Ration A subsequently showed a very uniform sequence of the symptoms which have been described above, several exceptional animals from the same litters as the others appeared to be unaffected by prolonged feeding of these rations or showed a minor degree of injury. The reason for these differences is not fully understood but is thought to be due to the occurrence of coprophagy in some of the rats. The cages which were used throughout have raised wire mesh floors and no difficulty has ever been experienced with their use in this laboratory in depleting rats on vitamin B-low rations, death often occurring in 4 to 5 weeks. On the egg white rations, however, the feces although rarely diarrheal, tended to be bulky and sticky and caught easily on the mesh. Several of the rats were observed to eat them. Sinclair (1930) has reported that rats on "fat-free" diets show the dermal symptoms described by Burr and Burr (1929, 1930) only if consumption of feces is prevented. Because of the uncertain occurrence of this spontaneous absence of symptoms, whatever its explanation, it was found more trustworthy to produce pronounced symptoms in the rat first, on egg white rations, and then test the effects of various dietary changes. In harmony with the results on prevention with liver in the egg white rations, it was found that 10 per cent of liver did not effect a cure but, on the other hand, that practically no stages of dermal or nerve involvement or decline in body weight seemed to be too advanced, short of actual death, for recovery on 20 per cent of liver.

DISCUSSION

The swiftness of the onset of the first acute symptoms in young rats weaned from stock diets and fed rations high in egg white
H. T. Parsons

suggests that these symptoms are manifestations of a direct injury from this foodstuff rather than a nutritional deficiency in the usual sense of the term. However, mere digestive disturbances in themselves would seem to be ruled out as an explanation of their origin because of the quantitative nature of the protection afforded by liver even when this is fed previously. These early symptoms strikingly resemble the disorder produced by cystine feeding, and there is the further analogy that cystine injury has been prevented by the use of yeast concentrate in the ration (Cox and Hudson, 1930).

The later dermal and nervous manifestations of more insidious onset, which occur on egg white Ration A after an apparent recovery from the first acute disorder, have no counterpart in any symptoms so far reported from cystine feeding. Injury, however, rather than a simple deficiency is indicated by the fact that the symptoms occur less early and in milder form with 20 or 40 per cent of egg white in the ration than with 66 per cent. The assumption must be made in drawing this conclusion that no protective factor is introduced with the sucrose used in diluting the egg white. On the other hand, the symptoms are as clear cut and uniform as for most of the deficiency diseases and may be prevented or cured by a definite concentration of liver in the ration. The resemblance of these symptoms of slow onset to those of pellagra is most striking and cannot be ignored in spite of the fact that 20 per cent of a dried yeast rich in vitamin G is included in the ration, and that dried egg white itself is known to be potent in the antidermatitis factor (Aykroyd and Roseoe, 1929). Complex dietary relationships have been shown in the past to be responsible for various anomalous results in nutrition experiments. The injurious effects on reproduction of adding ferric chloride (Waddell and Steenbock, 1928) or a high percentage of lard (Mattill, 1927; Evans and Burr, 1927) to otherwise adequate rations have been explained on the basis of a destruction of vitamin E in diets apparently containing an adequate amount of this vitamin. While unquestionable instances of unusual vitamin requirements on a given diet, or of lessened absorption or utilization of a vitamin, cannot so readily be cited, such conditions are not inconceivable. They might perhaps furnish as tenable hypotheses as postulating a new deficiency disease to account for the symptoms which so strikingly resemble pellagra in the present
Physiological Effects of Egg White

experiment. Norris and Ringrose (1930) attribute the pellagrous-like syndrome in chicks on an egg albumin ration to the intense requirement of this species for vitamin G. The results of Underhill and Mendel (1925, 1928) on the dietary deficiency canine disease resembling black tongue have been interpreted to indicate that pellagra may originate in more than one way. Reader (1930) has suggested that pellagra may be due to a combined deficiency of vitamin B₂ and a third as yet unidentified component of the vitamin B complex.

It is of interest to note that work by Sullivan and Dawson (1920-21) suggested that the sulfur metabolism is abnormal in acute cases of pellagra. They considered that the decrease in the normal sulfocyanate content of the saliva and urine of patients with active pellagra might be interpreted as an indication of the relative failure of detoxification by means of the -SH radical.

The results herein recorded confirm Bateman (1916) in suggesting caution in the use of as large quantities of raw egg white in invalid feeding as has been the common practice in many hospitals in the past. Furthermore the fact that many cases of eczema in children have been observed to be associated with a sensitization to egg white raises the question as to whether the early introduction of egg white into the somewhat restricted dietary of the child may perhaps need to be safeguarded with protective foods in somewhat the same way as its introduction into the diet of the rats in the present experiment.

SUMMARY

A nutritional disorder and death speedily result in the case of the majority of young rats weaned from stock rations when fed diets high in egg white, either raw or cooked, commercial, dried or fresh. The rats may be protected from these initial symptoms by even as little as 5 per cent of dried liver fed for 3 days before the beginning of the egg white diet.

On a ration containing 66 per cent of dried egg white, either raw, Chinese, or from raw fresh eggs, some symptoms later develop in the rats surviving the first few weeks which strikingly resemble those of pellagra even though the rations contain 20 per cent of potent dried yeast. These symptoms may be prevented or cured by 20 per cent of dried beef liver but not by 10 per cent.
Lard and raw linseed oil are not effective either in preventing or in curing the symptoms.

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Helen T. Parsons and With the cooperation of Eunice Kelly


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