PROTEIN ANABOLISM OF ORGANS AND TISSUES
DURING PREGNANCY AND LACTATION*

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It has been demonstrated that during a fast the various organs and tissues of the body lose protein at very different rates, some rapidly, others slowly, and others not at all (1). A similar disparity was found in the rate of gain in the protein content of different organs on refeeding after a fast (2). The significance of these differences in the various organs is not always obvious and this is especially true in the case of the liver, the organ in which the greatest rate and degree of change were observed. One of the reasons that led us to measure the total protein and organ protein content of pregnant and lactating rats was the hope that further information might be obtained as to the rôle of the liver in protein metabolism, but the principal incentive was the fact that gestation and lactation provide an opportunity to observe the effect of a drastic alteration in the conditions under which the processes of protein metabolism are ordinarily conducted. During pregnancy the formation of the embryos draws from the maternal blood the materials required for protein formation, while at the same time the enlargement of the uterus and formation of the placentas require a considerable preponderance of protein anabolism over catabolism. During lactation the whole of the rapidly increasing protein content of the litter is transferred through the milk proteins from the mother to the young. If in the non-pregnant, non-lactating female rats we find what part of the total protein of the body is allocated to the heart, kidney, liver, carcass, etc., we shall be able on comparing this control

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distribution with the distribution in the bodies of pregnant and lactating rats to answer the question as to what changes in protein distribution have occurred in the maternal body under these quite singular conditions.

100 female rats from 90 to 100 days of age were divided into five groups of twenty rats each in such a manner that the average body weight per rat in each group was 150 gm. on the day on which a diet containing 16 per cent of protein with adequate vitamin and mineral content was started. One group was sacrificed at once, another after 18 days, and another 31 days after the diet was begun. These were the three control groups and the increase in protein content over the period of observation measured the growth of protein in non-pregnant females. There were two experimental groups. From a number of females that had been kept with males for the previous 5 days two groups of twenty pregnant rats were chosen, each of which had an average body weight of 150 gm. when started on the 16 per cent protein diet. The rats of one of these groups were killed 18 days later when, on the average, they were at the 20th day of pregnancy. Those of the other groups went to term and were killed on the 31st day when, on the average, they had been giving milk to their young for 10 days. Since both the litters of the lactating rats and the embryos of the pregnant rats had grown solely on food derived from their mothers, their protein content was determined and added to the maternal protein. The total body and organ weights are given in Table I and the corresponding protein quantities in Table II.

1 The diet contained 16 per cent of casein, 9 per cent of yeast, 2 per cent of alfalfa, 10 per cent of sardine oil, 15 per cent of lard, 44 per cent of cornstarch, and 4 per cent of the Osborne-Mendel salt mixture (3). An attempt was made to determine the protein content of the air-dry casein and yeast. The total nitrogen concentrations were 13.26 and 8.39 per cent and the non-protein nitrogen concentrations 0.32 and 2.91 per cent respectively. Three methods for precipitating the protein, washing, extracting the fat, and drying were used and the estimates made either by direct weighings or by nitrogen determinations. We were not satisfied that any of these methods gave entirely reliable results but on averaging all our observations we concluded that the best estimate for the protein content of the air-dry casein was 79.1 per cent. In the case of the yeast the average protein content was found to be 46.0 per cent but consideration of the availability as food led us to reduce this estimate to 31.3 per cent. According to these figures the protein content of the diet is 15.86 per cent.
### TABLE I

*Average Weight in Gm. per Rat of Organs and Tissues of Pregnant, Lactating, and Control Groups of Twenty Rats with an Average Body Weight of 150 Gm. at 0 Days*

<table>
<thead>
<tr>
<th></th>
<th>Initial control at 0 days</th>
<th>Pregnancy at 18 days</th>
<th>Control for pregnancy at 18 days</th>
<th>Lactation at 31 days</th>
<th>Control for lactation at 31 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight of mothers</td>
<td>150</td>
<td>204</td>
<td>172</td>
<td>162</td>
<td>179</td>
</tr>
<tr>
<td>Weight of young</td>
<td></td>
<td>27.057</td>
<td>179</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total weight</td>
<td>150</td>
<td>231.057</td>
<td>172</td>
<td>236.900</td>
<td>179</td>
</tr>
<tr>
<td>Uterus</td>
<td>0.290</td>
<td>10.768</td>
<td>0.383</td>
<td>(0.326)</td>
<td>0.387</td>
</tr>
<tr>
<td>Alimentary tract, etc.</td>
<td>34.751</td>
<td>30.965</td>
<td>28.037</td>
<td>26.708</td>
<td></td>
</tr>
<tr>
<td>Drawn blood, † serum</td>
<td>2.876</td>
<td>3.450</td>
<td>2.935</td>
<td>3.040</td>
<td>2.876</td>
</tr>
<tr>
<td>&quot; clot</td>
<td>2.432</td>
<td>2.345</td>
<td>2.500</td>
<td>2.465</td>
<td>2.452</td>
</tr>
<tr>
<td>Heart</td>
<td>0.519</td>
<td>0.623</td>
<td>0.573</td>
<td>0.582</td>
<td>0.597</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.995</td>
<td>1.114</td>
<td>1.076</td>
<td>1.055</td>
<td>1.089</td>
</tr>
<tr>
<td>Carcass ‡</td>
<td>101.550</td>
<td>145.700</td>
<td>132.900</td>
<td>118.750</td>
<td>137.500</td>
</tr>
</tbody>
</table>

* The alimentary tract, etc., includes the entire abdominal and pelvic contents, except the kidneys, liver, and uterus. All visible abdominal and pelvic fat was included.

† Drawn blood is all the blood that could be obtained from the cut abdominal aorta of the anesthetized rat while the heart was still beating. After centrifuging at high speed the serum and clot were separated and weighed.

‡ The carcass is the whole rat after exsanguination, with the heart excised, stripped of all abdominal and pelvic organs and all visible fat.

### TABLE II

*Average Protein Content in Gm. per Rat of Organs and Tissues of Pregnant, Lactating, and Control Groups of Twenty Rats with an Average Body Weight of 150 Gm. at 0 Days*

<table>
<thead>
<tr>
<th></th>
<th>Initial control at 0 days</th>
<th>Pregnancy at 18 days</th>
<th>Control for pregnancy at 18 days</th>
<th>Lactation at 31 days</th>
<th>Control for lactation at 31 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein in mothers</td>
<td>23.546</td>
<td>29.446</td>
<td>27.325</td>
<td>26.525</td>
<td>29.573</td>
</tr>
<tr>
<td>&quot; young</td>
<td>2.072</td>
<td></td>
<td>9.429</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total protein</td>
<td>23.546</td>
<td>31.518</td>
<td>27.325</td>
<td>35.954</td>
<td>29.573</td>
</tr>
<tr>
<td>Maternal protein</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uterus</td>
<td>0.040</td>
<td>0.822</td>
<td>0.049</td>
<td>(0.051)</td>
<td>0.055</td>
</tr>
<tr>
<td>Alimentary tract, etc.</td>
<td>1.631</td>
<td>1.809</td>
<td>1.447</td>
<td>1.858</td>
<td>1.685</td>
</tr>
<tr>
<td>Drawn blood, serum</td>
<td>0.166</td>
<td>0.185</td>
<td>0.196</td>
<td>0.140</td>
<td>0.185</td>
</tr>
<tr>
<td>&quot; clot</td>
<td>0.712</td>
<td>0.714</td>
<td>0.743</td>
<td>0.668</td>
<td>0.804</td>
</tr>
<tr>
<td>Heart</td>
<td>0.083</td>
<td>0.103</td>
<td>0.098</td>
<td>0.097</td>
<td>0.101</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.161</td>
<td>0.177</td>
<td>0.177</td>
<td>0.173</td>
<td>0.183</td>
</tr>
<tr>
<td>Liver</td>
<td>1.256</td>
<td>1.602</td>
<td>1.194</td>
<td>1.330</td>
<td>1.393</td>
</tr>
<tr>
<td>Carcass ‡</td>
<td>19.497</td>
<td>24.034</td>
<td>23.421</td>
<td>22.208</td>
<td>25.167</td>
</tr>
</tbody>
</table>
Since at the beginning all the groups were identical, we can subtract the 23.5 gm. of total protein they then contained from the quantities found 18 and 31 days later. In the control groups the increase is the new protein formed during growth and in the pregnant and lactating groups the added protein is the combined result of maternal growth and the growth of the young. Table II shows that in the controls there was an increase of 3.8 gm. of protein in 18 days and of 6.0 gm. in 31 days, while in the pregnant groups the increase was 8.0 gm. and in the lactating groups 12.4 gm. of protein. Pregnancy alone is therefore responsible for the formation of 4.2 gm. of new protein, while on the 10th day of lactation 6.4 gm. of protein more than the amount to be anticipated from maternal growth had been laid down. Under both conditions the rate of protein anabolism is more than doubled. It was not possible to get reliable food measurements in the lactating group but in the pregnancy group the total protein taken in the food during 18 days was 34.8 gm. per rat and, since there was a new formation of 8 gm. of protein, 23 per cent of the protein eaten was used for anabolism. In the corresponding control group 24.2 gm. per rat were eaten and of this amount 16 per cent was used in growth.

A comparison of Tables I and II shows that the gain in weight during pregnancy and lactation is out of proportion to the gain in protein, so that the concentration of total protein per 100 gm. of total weight falls during pregnancy and lactation relatively to the controls. This is largely due to the high water content of the uterine contents in pregnancy (the embryos contained 7.7 per cent of protein) and of the 10 day-old litters (the protein concentration of the litters was 12.6 per cent). But this is not the only reason, for, if we consider the protein concentration in the organs and tissues of the mother alone, it will be noted that with the exception of the alimentary tract, and the carcass in the lactating group, there is a general reduction in protein per 100 gm. of organ or tissue weight. The order and extent of this protein dilution are shown in Figs. 1 and 2.

This reduction in protein concentration cannot be ascribed to an increase in the fat content of the organs and tissues in pregnancy and lactation. Inspection suggested a decrease of fat content and this is borne out by the fact that the alimentary
PREGNANCY
CONCENTRATION OF PROTEIN (PROTEIN PER 100 GMS.
FRESH WEIGHT OF ORGAN OR TISSUE) RELATIVE TO
CONCENTRATION IN CONTROLS. (CONTROLS = 0).

LACTATION
CONCENTRATION OF PROTEIN (PROTEIN PER 100 GMS.
FRESH WEIGHT OF ORGAN OR TISSUE) RELATIVE TO
CONCENTRATION IN CONTROLS. (CONTROLS = 0).
tract in whose weight all visible abdominal and pelvic fat is included is an exception to the general rule and has a higher concentration of protein than the controls. It is therefore highly probable that the reduction in protein concentration is due to an increased water content of the maternal tissues, though it cannot be concluded that this is a phenomenon always characteristic of pregnancy and lactation because our observations were made under one set of dietary conditions, and the food given contained only 16 per cent of protein, almost all in the form of casein.

The concentration of protein in the organs and tissues is in itself a measurement whose significance is ambiguous, since it may be altered by changes in either water or fat content. There is no such doubt when we consider the total protein content of the body and find what proportion of that total is allocated to the various organs and tissues, for protein is the essential operating machinery of the body and the proportion distributed to each organ can be regarded as an indication of its significance in the total economy. Our reason for this statement rests on the observation that when conditions are devised that increase or decrease the work of the heart or kidney we have found a corresponding rise or fall in the proportion of the total protein found in these organs, so that if time for adjustment is allowed the pattern of distribution of protein in the various parts of the body may be taken as an indicator of function. During pregnancy and lactation, on the diet we gave, the conditions with respect to protein are of such a nature as to necessitate an unusual economy in the distribution of the total available amount. During pregnancy the maternal organism becomes subsidiary to the needs of the rapidly growing parasitic embryos, and throughout lactation the drain on the maternal resources is continued through the provision in the milk of all of the protein used by the young. Under such conditions deviations from the distribution in the organs and tissues of control rats subjected to no such drain are of interest as a rough indication of their relative functional importance. This distribution of maternal protein (total protein less the protein of the uterus, the embryos, and the young) in pregnancy and lactation relative to that found in the controls is shown in Figs. 3 and 4.

The results show that in pregnancy the serum and clot of the drawn blood, the kidney, and the carcass have smaller proportions
**Pregnancy**

**DISTRIBUTION OF PROTEIN** (PROTEIN PER 100 GMS.
MATERNAL PROTEIN) RELATIVE TO DISTRIBUTION IN CONTROLS. (CONTROLS = 0).

- **Fig. 3**

**Lactation**

**DISTRIBUTION OF PROTEIN** (PROTEIN PER 100 GMS.
TOTAL MATERNAL PROTEIN) RELATIVE TO DISTRIBUTION IN CONTROLS. (CONTROLS = 0).

- **Fig. 4**
of the total protein assigned to them and that other organs, the alimentary tract and the liver, have considerably more than the controls. The increase in the alimentary tract may be a result of the work hypertrophy that has been shown to follow an increase in the bulk of food consumed (4). Whether the decrease in serum, clot, and carcass protein is a depletion effect arising because the gastrointestinal tract was mechanically incapable of carrying the quantity of food containing only 16 per cent of protein that was required to meet the increased demand is a question that can be answered by observing the effect of foods with higher protein concentrations. If with increase in total protein consumption we no longer find any decrease in the amount of protein allocated to these tissues, the simple depletion hypothesis is validated. But if this decrease is found even when more than adequate quantities of protein are taken, we must look for some other mechanism. These considerations apply also to the decrease in serum, clot, and carcass protein proportions during lactation, while the increase in the kidney protein in lactation suggests a greater consumption and catabolism of protein, since in other experiments we have found that the proportion of protein in the kidney varies with nitrogen excretion.

The unexpected and most interesting result is the 28 per cent increase in the amount of protein allocated to the liver in pregnancy, unexpected because in other experiments in which the effect of dietetic or metabolic changes has been observed there has been agreement in the direction of change in kidney and liver protein changes (5) and interesting because the reason for the increase in liver protein is uncertain. One possibility is that it represents a store of protein laid down against the need of protein for milk formation, and that this storage is a special adaptation for the preservation of the species developed in rodents under conditions of life in which a temporary shortage of protein may be a frequently recurring event during lactation. But if the decrease in blood and carcass protein is the effect of a depletion of protein, this storage must be a very special adaptation, since as a rule there is a very rapid decrease in liver protein whenever the protein intake is inadequate (6). The other possibility is that the increase is the result of a work hypertrophy of the liver during pregnancy. But we have no knowledge as to the nature of this
hypothetical work. At best we can relate it to the increase in anabolic activity in pregnancy and suppose that it may be some energy-requiring preparation of material utilized by the embryos. As between storage or work hypertrophy it may be hoped that total protein and organ protein determinations on pregnant rats given protein quantities from bare maintenance to surplus amounts will be decisive. These observations are now being made.

**SUMMARY**

1. The rate of protein anabolism in growing rats is more than doubled towards the end of pregnancy and on the 10th day of lactation.

2. The concentration of protein per 100 gm. of organ or tissue weight is most reduced in the serum and in successively less degree in the liver, blood clot, kidney, and heart in both pregnancy and lactation on a diet that contained 16 per cent of protein.

3. The proportion of the total maternal protein allocated to the serum, blood clot, kidney, and carcass is reduced in pregnancy. In lactation the serum, blood clot, and to a slight degree the carcass have less than the usual proportions of the total protein. In both pregnancy and lactation the alimentary tract contains more than the usual proportion of protein.

4. There is a 28 per cent increase in the proportion of protein assigned to the liver in pregnancy.

**BIBLIOGRAPHY**

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