THE NUCLEIC ACID CONTENT OF FETAL RAT LIVER*

BY I. GESCHWIND† AND CHOII HAO LI
(From the Institute of Experimental Biology, University of California, Berkeley)
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It has been shown by various investigators that embryonic tissues are richer in nucleic acid than are adult tissues (1). The distribution of the two types of nucleic acids (ribonucleic acid (RNA) and desoxy-ribonucleic acid (DNA)) is also known to be different in embryonic and adult tissues and in different tissues. For instance, muscle and heart are low in ribonucleic acid concentration, whereas liver and pancreas have a high content of this nucleic acid. The ratio of RNA to DNA is smaller in the liver of sheep embryos than in that of the adult animal. Caspersson and others (2) have suggested that these changes are in some way related to protein synthesis for purposes of growth or of secretion.

Systematic determinations of the changes in nucleic acid concentration in embryonic mammalian liver have not been conducted. Masing (3), working with rabbit liver, found that a decrease in the nucleoprotein phosphorus per unit of nitrogen of the liver occurred from the 4th week of gestation to the adult period; the ages of the animals were, however, not accurately determined. Dumm (4) showed a decrease of "residual phosphorus" in the fetal liver of rats during the later period of gestation; the author did not determine separately the RNA-P and DNA-P. Dumm's results, expressed as residual phosphorus, may be accepted as being due to nucleoprotein phosphorus, because the phosphoprotein phosphorus (the only other phosphorus fraction present in residual phosphorus) is always small in comparison with that for nucleic acids.

In the present experiments fetal rat livers from the 16th to the 21st prenatal day were employed. The nucleic acids in the tissue were fractionated into RNA and DNA. It will be seen that the ratio RNA:DNA is relatively constant from the 16th to the 19th day and that it increases at the 20th day.

EXPERIMENTAL

Pregnant rats of the Long-Evans strain were used; the dates of breeding were accurately determined by the presence of sperm in the vagina.

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NUCLEIC ACID CONTENT OF LIVER

The animals were anesthetized with nembutal; the fetuses were quickly removed from the uterus and weighed after being dried on filter paper. The livers were extirpated and immediately frozen in a weighing bottle with an acetone-dry ice mixture. Between the time of the death of the animal and the preparation of the livers for nucleic acid determinations, the tissues were covered and stored in the ice chest of a refrigerator. This interval was never greater than 1 hour.

The methods for nucleic acid determinations were modeled after those of Schmidt and Thannhauser (5) and of Schneider (6). The method of Fiske and Subbarow (7) was employed for phosphorus analysis.

<table>
<thead>
<tr>
<th>Day of gestation</th>
<th>No. of pregnant rats</th>
<th>No. of fetuses</th>
<th>Total weight of fetus</th>
<th>Total weight of liver</th>
<th>Ratio, Liver/Fetus</th>
<th>No. of determinations</th>
<th>P per 100 gm. dry extracted liver</th>
<th>Ratio, RNA-P/DNA-P</th>
</tr>
</thead>
<tbody>
<tr>
<td>16th</td>
<td>15</td>
<td>134</td>
<td>0.50</td>
<td>26</td>
<td>0.062</td>
<td>7</td>
<td>1109 ± 50*</td>
<td>0.98</td>
</tr>
<tr>
<td>18th</td>
<td>12</td>
<td>105</td>
<td>1.60</td>
<td>95</td>
<td>0.060</td>
<td>5</td>
<td>973 ± 68</td>
<td>0.85</td>
</tr>
<tr>
<td>19th</td>
<td>7</td>
<td>58</td>
<td>2.10</td>
<td>140</td>
<td>0.067</td>
<td>3</td>
<td>1137 ± 19</td>
<td>0.93</td>
</tr>
<tr>
<td>20th</td>
<td>9</td>
<td>80</td>
<td>2.90</td>
<td>175</td>
<td>0.060</td>
<td>6</td>
<td>988 ± 20</td>
<td>1.43</td>
</tr>
<tr>
<td>21st</td>
<td>3</td>
<td>25</td>
<td>4.50</td>
<td>245</td>
<td>0.055</td>
<td>1</td>
<td>854</td>
<td>1.94</td>
</tr>
</tbody>
</table>

*Mean ± standard error.

Results

As is shown in Table I, the fetal body weight increases steadily throughout the period studied. It is of interest to note that the values are higher than those of Dumm (4), whose data agree with those reported by Donaldson (8). This is probably due to the improved nutritional state of our animals. There is a slight increase in the liver weight, as expressed in percentage of body weight from the 15th to the 19th day of gestation, followed by a slight decrease until about the day of birth, after which a sudden drop occurs.

The last three columns in Table I give the values for RNA-P, DNA-P, and their ratios. Assuming a molecular weight for RNA of 1303 and of 1253 for DNA, the amount of phosphorus is 9.52 and 9.89 per cent respectively; so that if equal moles of RNA and DNA are present, the ratio will be 0.96. It may be seen that both RNA-P and DNA-P are relatively constant from the 16th prenatal day to the 19th, and the ratios suggest that they are present in 1:1 molar relationship. The mean value for RNA-P in this period is 1073 mg. of P per 100 gm. of extracted dry tissue and that for DNA-P 1165 mg. of P.
There is a gradual fall of the RNA content from the 20th prenatal day to 40 days after birth (Table II). The changes in the DNA-P are more striking. Following the 19th prenatal day, a precipitous fall in the level of DNA occurs, changing from 1223 mg. to 441 mg. per cent just before the day of birth. The more gradual decrease from the 1st day of birth to 40 days of age is still more rapid than the rate of decrease of RNA during the same period (Table II).

The marked variation in the ratio of RNA-P to DNA-P observed from the 20th prenatal day to the 5th day after birth is not significant, and the ratio is about 1.45. The value obtained for the liver of 40 day-old male rats is 2.83.

### Table II

<table>
<thead>
<tr>
<th>Age</th>
<th>No. of rats</th>
<th>Average body weight</th>
<th>Average liver weight</th>
<th>Ratio, liver/body weight</th>
<th>No. of determinations</th>
<th>P per 100 gm. dry extracted liver</th>
<th>Ratio, RNA-P/DNA-P</th>
</tr>
</thead>
<tbody>
<tr>
<td>days</td>
<td></td>
<td>gm.</td>
<td>gm.</td>
<td></td>
<td></td>
<td>RNA mg.</td>
<td>DNA mg.</td>
</tr>
<tr>
<td>1</td>
<td>12</td>
<td>6.1</td>
<td>0.31</td>
<td>0.051</td>
<td>1</td>
<td>672</td>
<td>469</td>
</tr>
<tr>
<td>5</td>
<td>12</td>
<td>12.9</td>
<td>0.45</td>
<td>0.035</td>
<td>2</td>
<td>602</td>
<td>370</td>
</tr>
<tr>
<td>40</td>
<td>4</td>
<td>115.0</td>
<td>4.60</td>
<td>0.040</td>
<td>2</td>
<td>532</td>
<td>188</td>
</tr>
</tbody>
</table>

### Discussion

Davidson (1) has summarized the data obtained by different authors for the nucleic acid content of rat liver and other tissues. The ratio RNA-P:DNA-P for rat liver was found to vary from 1.9 to 4.6, depending upon the method of determination, age, nutritional condition, etc. The same author also obtained a value of 2.2 for fetal rat liver (age?), compared to an adult value of 4.0. In an earlier paper, Davidson and Waymouth (9) reported a ratio of 1.5 for the liver of rat fetuses 1 to 2 days before parturition, with a value of 4.3 for the adult animal. The fact that the livers of rat fetuses have a smaller RNA-P:DNA-P ratio than that for adult tissue is confirmed by the present experiments. Our value for the fetal liver of rats from the 16th to the 19th prenatal day is about 0.92, and it increases to 2.83 for the liver of rats 40 days of age.

Schneider (10) has determined the RNA-P:DNA-P ratio for rat liver tumors and compared it with that found in adult rat liver. It was found that the ratio for tumor tissue is much lower than non-tumor liver, the

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1 This decrease in DNA-P is less striking if the total amount of DNA-P present is considered. The authors are grateful to the referee who pointed out that a large proportion of this drop is undoubtedly due to the increase in the cytoplasm and the proportionate decrease of the nuclear volume as the mitotic rate decreases.
value for the tumor being 0.81, in contrast to the normal ratio of 2.49. It appears that the rapidly growing livers, either of tumor or fetal origin, possess a nearly equal molar quantity of DNA and RNA.

The partition of nucleic acids in the regenerating rat liver has been recently investigated (11, 12). Novikoff and Potter (11) found that there is an apparent correlation between the period of rapid growth and the increase in RNA concentration. No consistent changes in DNA content occurred in the regenerating period. Our results, as shown in Fig. 1, indicate more marked changes in the concentration of liver DNA from the prenatal to the postnatal period than in the values for RNA. It is clear, however, that the fetal liver has the highest concentration of total nucleic acids during the most rapid growing period of the tissue from the 16th to the 19th prenatal day.

**SUMMARY**

1. The concentration of ribonucleic (RNA) and desoxyribonucleic (DNA) acid phosphorus in the liver of rat fetuses has been determined.
2. The results demonstrate a constant RNA content from the 16th to the 20th prenatal day, followed by a gradual decrease to the juvenile level. The concentration of DNA-P is constant from the 16th to the 19th day, followed by a decrease to the juvenile level.
3. The ratio RNA-P:DNA-P has been shown to be relatively constant.
at about 0.9 from the 16th to the 19th day; it then increases gradually, a value of 2.9 being found at 40 days of age.

BIBLIOGRAPHY

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I. Geschwind and Choh Hao Li


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