The Effect of Tumor Implants on Chick Embryo Liver Catalase Activity*

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Several possible explanations have been suggested for the drastic decreases in liver catalase activity produced by tumor implants in mice and rats (1, 4, 5, 9). Since no specific mechanism has been demonstrated, the alternative hypotheses and evidence are presented below:

1. There may be an actual interference with the synthesis of catalase necessary to maintain the normal concentration in the liver. However, in a previous paper (1) it was shown that a significant number of rats failed to show a decreased catalase activity in the presence of large tumors.

2. One possible mechanism of interference is the production by the tumor of some toxic substance which affects the liver catalase activity. Recent work (6) has led to the extraction of a fraction of low molecular weight from tumors which, when injected intraperitoneally, lowered liver catalase activity of normal mice.

3. There may be abstraction from the circulation of some substance necessary for the maintenance of a normal liver catalase activity.

4. Because of the increased protein requirement of the animal with a growing tumor, experiments have been performed by varying the level of dietary protein (9). Increased levels of protein had little effect on the liver catalase of tumor-bearing rats.

This work was undertaken to determine the effect of tumor implants upon the liver catalase activity during embryonic development. It was felt that the avian egg would provide a fully adequate system for testing the effect of the tumor on liver catalase, since it is free from the variable of a possible, but undetected, essential limiting substance in standard laboratory diets. Furthermore, the physiological adaptability of the embryo might allow it to adjust its metabolic processes to meet the demands imposed by both the normal developmental process and the growth of the tumor.

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MATERIALS AND METHODS

Embryonated New Hampshire Red eggs, supporting growth of implants of Brown-Pearce carcinoma and Jensen fibrosarcoma on the chorioallantoic membrane, were used for the liver catalase measurements. The desired tumor tissue was implanted into eggs which had been incubated for 8 days at 37.5° C. The procedure was that reported by Schechtman et al. (8). The embryos were obtained after the eighteenth day of incubation. Sham-operated groups and embryos inoculated with tumor tissue, but showing no growth of the implant, were used as control groups to determine the normal enzymatic activity.

The tumor was dissected from the chorioallantoic membrane and weighed; the liver was removed, weighed, sealed, and immediately frozen. The weight of the remaining carcass was also determined. In most cases the liver samples were pooled into groups classified according to the amount of tumors found. The pooled or single liver samples were homogenized at 0° C. in M/15 phosphate buffer at pH 7.0. Catalase activity was determined by the procedure reported in a previous publication (1); aliquots of the homogenate were analyzed for nitrogen by the customary semimicro-Kjeldahl method.

RESULTS

Sixty-two chick embryos were collected and separated into groups as shown in Table 1. Nitrogen and catalase activity values are expressed on various bases to facilitate a more accurate interpretation of the data. A portion of the data is further presented in Chart 1. The changes produced by the growth of the tumor may be summarized as follows:

1. An increase in rate of growth of the liver is effected. This is accompanied by an approximately proportionate increase in the total liver nitrogen.

1 We are indebted to Dr. A. M. Schechtman, Elia C. Berkozitz, and Melvin J. Cohen for their generosity and aid in providing the experimental material used for the analytical determinations.
TABLE 1
THE EFFECTS OF TUMOR IMPLANTS ON THE CHICK EMBRYO LIVER

<table>
<thead>
<tr>
<th></th>
<th>Brown-Pearce control animals</th>
<th>Nontake group</th>
<th>Brown-Pearce carcinoma 0-0.1 per cent</th>
<th>Brown-Pearce carcinoma 0.8-3 per cent</th>
<th>Jensen sarcoma 0.8-3.5 per cent</th>
<th>Jensen sarcoma 4.7-7.3 per cent</th>
<th>Jensen sarcoma 9.4-13 per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver, weight per cent</td>
<td>2.68</td>
<td>2.62</td>
<td>2.60</td>
<td>3.37</td>
<td>3.21</td>
<td>5.40</td>
<td>3.54</td>
</tr>
<tr>
<td>Average value of groups</td>
<td>2.65</td>
<td>5.41</td>
<td>3.27</td>
<td>5.77</td>
<td>3.55</td>
<td>4.75</td>
<td>5.77</td>
</tr>
<tr>
<td>Liver nitrogen, mg/100 gm embryo weight</td>
<td>56</td>
<td>42</td>
<td>77</td>
<td>81</td>
<td>87</td>
<td>89</td>
<td>87</td>
</tr>
<tr>
<td>Average</td>
<td>59</td>
<td></td>
<td>91</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>22.5</td>
<td></td>
<td>24</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver catalase activity units/ 100 gm embryo wt.</td>
<td>90</td>
<td>95</td>
<td>89</td>
<td>81</td>
<td>105</td>
<td>115</td>
<td>106</td>
</tr>
<tr>
<td>Average</td>
<td>92.5</td>
<td>109</td>
<td>125</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver catalase activity units/ mg Liver N</td>
<td>1.59</td>
<td>1.53</td>
<td>1.49</td>
<td>1.06</td>
<td>1.20</td>
<td>1.47</td>
<td>1.85</td>
</tr>
<tr>
<td>Average</td>
<td>1.56</td>
<td></td>
<td>1.55</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver catalase activity units/ gm liver</td>
<td>33</td>
<td>35</td>
<td>34</td>
<td>26</td>
<td>38</td>
<td>40</td>
<td>31</td>
</tr>
<tr>
<td>Average</td>
<td>34</td>
<td>32</td>
<td>39</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average tumor weight per cent group</td>
<td>0</td>
<td>0.2</td>
<td>1.6</td>
<td>1.8</td>
<td>4.8</td>
<td>1.0</td>
<td>2.9</td>
</tr>
<tr>
<td>Range of group tumor size in percentages</td>
<td>0</td>
<td>0.01-</td>
<td>0.8-</td>
<td>0.7-</td>
<td>3.5</td>
<td>0.8-</td>
<td>3-</td>
</tr>
</tbody>
</table>
2. There is a greater proportionate increase in liver nitrogen than in liver catalase activity.

3. Liver catalase activity increases if calculated per hundred grams of body weight but shows values below those of the control groups when calculated on a unit nitrogen basis or on a fresh tissue weight basis.

4. The stimulation of liver growth and nitrogen incorporation occurs with small amounts of tumor growth. Stimulation of nitrogen incorporation in the liver is not directly proportional to tumor mass.

The increases in liver fresh weight and nitrogen are interpreted as an increase in the rate of growth of the liver caused by the influence of the tumor. This is provisionally interpreted as a readjustment on the part of the liver in an effort to meet the metabolic requirements of the tumor.

The data presented herein indicate increased total amounts of liver catalase in the chick embryo which is supporting the growth of a tumor. It is suggested that the effect of the tumor is to create either qualitative or quantitative changes in intermediary metabolism patterns. The adult rat may not mediate these metabolic changes as readily as the chick embryo. Evidently the embryo possesses the nutritional adequacy and/or the synthetic ability to mediate a more rapid, or a different pattern of, metabolism in response to the tumor growth.

Friedberg et al. (3) and Borsook et al. (2) have shown that the rate of amino acid incorporation into proteins is much greater in the fetus than in the adult animal. Zamecnik et al. (10) have also shown that the rate of incorporation of labeled amino acids into the proteins of surviving hepatoma nodules was 7 times that of slices of normal livers and 2.5 times that of slices from the nonmalignant portions of the hepatoma-containing livers.

The data do not support a tendency to establish an enzyme level in the liver of the host similar to the low catalase level found in the growing tumor (5). It is felt that it would be reasonable to assume that the tumor causes an increase in the quantitative demand for certain enzymes beyond the normal requirements of the animal. Rosenthal et al. (7) have shown that the rate of restoration of liver arginase activity after partial hepatectomy of rats was geared to the endogenous protein catabolism of the animal and paralleled urinary nitrogen excretion. Arginase activity restoration was greater in the case of protein-starved animals. Thus, one could explain increased, decreased, and normal enzyme activity levels in terms of the metabolic demands imposed by tumor growth and capacity of the animal to synthesize enzymes. This, of course, assumes the synthesis and destruction of enzyme molecules in the processes of intermediary metabolism. Insufficient data prevent the evaluation of results in terms of new qualitative types of metabolism patterns.

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Future studies of the enzyme patterns in the tumor-bearing chick embryo may yield a more accurate interpretation of the effects of tumors on enzyme systems.

SUMMARY

1. The effects of chorioallantoic implants of Brown-Pearce carcinoma and Jensen fibrosarcoma...
on liver catalase activity in the chick embryo have been studied.

2. The expression of liver catalase activity on a unit nitrogen basis shows decreased enzymatic activity, but the total quantity of liver catalase per unit weight of chick embryo plus tumor shows increased activity. The data suggest that tumor growth does not interfere with catalase synthesis.

3. Tumor growth stimulates incorporation of liver nitrogen to a greater extent than the increase in total liver catalase activity.

REFERENCES


The Effect of Tumor Implants on Chick Embryo Liver Catalase Activity

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