Chemical Characteristics and Varying Degrees of Malignancy in Tumors of the Human Ovary

I. Oxygen Consumption and Lactic Acid Production*

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The present paper deals with the correlation of oxygen consumption and lactic acid production with the histologically determined grades of malignancy of tumors of the human ovary. This work is part of a planned search for any biological and biochemical properties of tumors that may vary with the grades of malignancy. Such a property might be regarded as one of the essential characteristics of the malignant process itself.

The concept of grade of malignancy, often termed degree of loss of tissue differentiation, requires some comment. That individual cases of cancer arising in the same organ have widely different rates of evolution is a clinical commonplace. That tumors, of certain tissues at least, display a varying microscopic structure which may be roughly correlated with the rate of spread of the disease is also accepted.

The papillary tumors of the ovary, especially the so-called “serous” variety, offer for many reasons an ideal source material for the study of the biology and biochemistry of grades of malignancy. These tumors are among the most “gradable,” for they grow as branching structures projecting freely into the interior of a fluid-filled space. The histology is, therefore, that of the tumor itself, relatively uninfluenced by effects of accommodation to an invaded normal, connective, or other tissue. As a result of this, the ovarian serous adenomas and adenocarcinomas can be arranged with fair success into a series of histological forms, ranging from the benign to the most malignant types. A second favorable feature of the ovarian tumors is that they are relatively bulky, and tissue can be obtained in amounts for repeated experiment.

The histological characteristics which are used to determine whether an ovarian papillary tumor composed of serous cells is benign or malignant and to provide the basis for classification into “grades” have been described elsewhere (12).

A systematic study of the correlation of histologically determined grades of malignancy with biological or biochemical properties, theoretically of such importance in oncology, seems not, however, to have been attempted. This neglect has stemmed, in part at least, from the frequently inconsistent correlation between histological grade and clinical end results.

Papillary serous tumors of the ovary reveal forms ranging from the earliest benign changes in the germinal epithelium to the most malignant types; they present an unbroken series of types with no abrupt structural transition to mark the point at which progress to a fatal termination may occur. It appears, then, that general biochemical characteristics such as those observed by Warburg and others (3, 6, 9–11, 14–16) as characteristically differentiating normal and tumor tissues could be used to distinguish between the grades of malignancy of these ovarian tumors.

MATERIALS AND METHODS

Tissue.—During a period of 8 years, 116 human gynecological tumors have been received for study; of this number, 51 were gradable ovarian tumors which were used primarily for this study. The ovarian tumors can be divided into two groups—namely, the ovarian papillary serous cystadenoma and cystadenocarcinoma and ovarian pseudomucinous cystadenoma and cystadenocarcinoma. For the purposes of comparison, however, some studies were carried out with epidermoid carcinoma of the cervix, and, in addition, a group of diversified tumors called “miscellaneous tumors” were also used.

Human gynecological tumors were placed on ice...
within minutes after excision and kept there until used for chemical studies. In virtually all cases, this tissue was in the Warburg vessel in less than ½ hour from the arrival of the tumor in the laboratory. The total time elapsed after removal from the patient until the tissue was in the Warburg vessel ranged from 1 to 2½ hours. In survival studies with these human gynecological tumors (to be reported elsewhere), it was found that the metabolic characteristics reported in this paper are not significantly decreased in as much as 6 hours of storage at +7° C.

Because of the variation of the amounts of epithelium and stroma of primary human tumors, the areas of the tissue used for chemical studies were always adjacent to those used for histological grading. As a further check on the homogeneity of tissue, alternate slices to those used in the Warburg flasks were fixed in 10 per cent neutral formalin. The formalin-fixed sections were stained with hematoxylin and examined microscopically by Dr. Margaret E. Long. The percentage of epithelium was estimated by measuring the approximate area of the tissue and that of the epithelium with an ocular micrometer.

TECHNIQUES FOR MANOMETRIC STUDIES

Flask content and procedure.—By the method of Umbreit (13), oxygen consumption was determined directly. The tumors were sliced into 0.5-mm. sections, and approximately 200 mg. of these slices was used for each Warburg vessel. The suspension medium was a Krebs-Ringer buffered solution (Krebs II) (8) to which, in some instances, 100 mg. per cent glucose (final concentration in vessel) was added. Readings were taken at 30-minute intervals for 2–3 hours; the bath temperature was 37.4° C.

The Warburg determinations were run in triplicate, and in most instances the values reported are the averages of the three. However, when the $Q_{O_2}$ of one of the triplicate vessels differed by more than 15 per cent from the average $Q_{O_2}$'s of the other two vessels, the results reported represent the average of the two values that were in agreement with each other. Deviations of this magnitude were infrequent, occurring only in about 15 per cent of the tumors examined.

Lactic acid determinations.—The lactic acid content of each Warburg vessel incubation mixture was assayed in duplicate according to the method of Barker and Summerson (1). The lactic acid production of the tissue was calculated from the lactic acid content prior to and subsequent to the 2-hour incubation at 37.4° C. The agreement of duplicate determinations was within 5 per cent.

RESULTS

THE OXYGEN UPTAKE AND LACTIC ACID PRODUCTION OF OVARIAN TUMORS

Ovarian papillary serous cystadenoma and cystadenocarcinoma.—An average $Q_{O_2}$ of 0.6 was obtained for the benign tumors and of 2.8 for the more malignant Grade III tumors (Table 1). The behavior of the Grade III tumor No. 25 appears to be an exception ($Q_{O_2}$ of 0.9 and 1.2); however, this may possibly be explained by its low epithelium content (cf. Table 1). Compared with a 60–90 per cent epithelium content for the other Grade III tumors, the specimen No. 25 had only 2–10 per cent epithelium. Another exception is the high $Q_{O_2}$ values obtained for both of the borderline tumors.

Oxygen consumption was generally higher in the absence of glucose than in its presence. Similar observations of a depression of oxygen consumption caused by physiological concentrations of glucose have been reported from a number of laboratories (2) working with ascites and other tumors of animal origin (10). In a few experiments with human ovarian tumors the addition of ATP in concentrations of 200 and 400 mg. per cent did not influence the depression caused by glucose.

In the absence of glucose, the lactic acid production was usually, but not consistently, greater for the malignant tumors than for the benign ones. On the other hand, the lactic acid production in the presence of glucose for the Grade III papillary tumors (Table 1) was invariably much greater than was obtained for the benign tumors. The average values in air for $Q_{O_2}$ were 1.5 for the benign tumors and 11.2 for the Grade III tumors. It is evident, therefore, that correlation with malignancy was obtained with the lactic acid production in the presence of added glucose, but not so consistently in its absence.

Similar determination of the oxygen consumption and lactic acid production of the ovarian papillary serous tumors were carried out in a gas phase of 100 per cent oxygen (Table 1). The $Q_{O_2}$ values in oxygen for the borderline Grades I, II, and III tumors were generally up to 50 per cent higher than the corresponding values in air. With the two benign tumors, however, there was no significant difference between the $Q_{O_2}$ values in air and oxygen. These results of the $Q_{O_2}$ values in a gas phase of oxygen can be correlated with malignancy, i.e., average value of 0.35 for the $Q_{O_2}$ of benign tumors, as compared with 4.0 for the Grade III tumors. The addition of glucose caused a very noticeable depression in the $Q_{O_2}$ of the malignant tumors and a less marked increase in oxygen uptake with the benign tumors. The latter observa-

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tion with the benign tumors is based solely upon the results with two tumors, both with very low QO\(_2\) values, and is therefore of dubious significance.

In a gas phase of 100 per cent oxygen and in the absence of glucose, the lactic acid production of the benign as well as malignant tumors was negligible. Addition of glucose to the incubation mixture resulted in an average QO\(_2\) of 1.0 for the benign tumors, as compared with 12.0 for the Grade III tumors. These results again show correlation of malignancy with the lactic acid production in the presence of added glucose.

Spontaneous tumors, being composed of variable mixtures of connective tissue and epithelium,

### TABLE 1

**OXYGEN CONSUMPTION AND LACTIC ACID PRODUCTION OF HUMAN PAPILLARY SEROUS CYSTADENOMA AND CYSTADENOCARCINOMA**

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* QO\(_2\)* represents the µl of oxygen consumed/mg dry weight tissue/hour at 37.4° C., in the indicated gas phase.

† QO\(_2\)* represents the µl of oxygen consumed/mg dry weight tissue/hour at 37.4° C. in the presence of added glucose, in the indicated gas phase.

‡ QLA represents the µg of lactic acid produced/mg dry weight tissue/hour at 37.4° C., in the indicated gas phase.

§ QLA represents the µg of lactic acid produced/mg dry weight tissue/hour at 37.4° C. in the presence of added glucose, in the indicated gas phase.

# Estimated microscopically from sections adjacent to those used for metabolic studies.

L = refers to left ovary.

R = refers to right ovary.
are heterogeneous. In addition to this heterogeneity there is an increase in the epithelium to stroma ratio in malignant human gynecological tumors as compared with the corresponding benign tumors. Because of this heterogeneity and variation in epithelium to stroma ratio, the percentages of epithelium present in a few of the papillary serous tumors were estimated (Table 1). As expected, the more malignant tumors were found to have a greater epithelium content than did the benign tumors. A method for elimination of the variable percentage of epithelium from the metabolic results is given in the discussion.

Calculation of the ratio for ovarian papillary serous tumors of the molecules of glucose fermented to those oxidized (16), especially in a gas phase of air, correlated with malignancy (Table 1). An average value of 8.5 ± 1.4 was obtained for benign tumors, as compared with 19.5 ± 5, 20.6 ± 2.6, and 15.1 ± 1.9 for the malignant I, II, and III, respectively.

Ovarian pseudomucinous cystadenoma and cystadenocarcinoma.—Low Q0, values in air (0.7 average) were obtained for benign tumors, as compared with 19.5 ± 5, 20.6 ± 2.6, and 15.1 ± 1.9 for the malignant I, II, and III, respectively.

In nine out of the fourteen benign tumors there was an increase in oxygen consumption in the presence of added glucose. The opposite behavior, namely, a depression in Q0, in the presence of glucose, was observed with four of the remaining tumors. No change in oxygen consumption in the presence or absence of glucose was obtained with the remaining benign tumor. The four malignant and one borderline tumors all showed a small increase in oxygen consumption in the presence of glucose. This behavior was in marked contrast to the general depression in Q0, in the presence of glucose obtained with the ovarian papillary serous tumors.

In the presence of glucose the lactic acid production was in most cases significantly greater than in the absence of glucose. However, the results of the lactic acid production were so variable that no correlation with malignancy can be seen. This is again in contrast to the correlation of Q0, with malignancy for the ovarian papillary serous tumors.

Comparable determinations of the lactic acid production and oxygen consumption in 100 per cent oxygen (Table 2) for the malignant tumors gave results similar to those obtained with the papillary serous tumors. Thus, approximately a 50 per cent increase in the Q0, values for the malignant tumors in oxygen as compared with air was observed. On the other hand, the benign tumors exhibited smaller (approximately 25 per cent), although erratic, increases in Q0, The lactic acid production in oxygen as compared with air decreased to zero in almost half of the benign tumors, and significantly decreased in the remainder of them. In the presence of added glucose the increase in lactic acid production was not so great as was observed in comparable determinations in air; the Q0, 's in oxygen were approximately two-thirds those obtained in air.

Calculations of the molecules of glucose fermented to molecules of glucose oxidized were made for ovarian pseudomucinous tumors in both air and oxygen (Table 2). The average of the values in a gas phase of air (11.6 ± 2) was within the range obtained for benign papillary tumors—namely, 8.5 ± 1.4. Comparable values in a gas phase of oxygen were also similar for both of the ovarian tumors.

The Oxygen Uptake and Lactic Acid Production of Other Gynecological Tumors

Epidermoid carcinoma of the cervix (primary and metastasis).—Cervical cancers are invasive, and samples of tissue from such tumors usually consist of a mixture of neoplastic cells and the invaded tissue. The structure that the malignant tissue takes in this region is dependent not only upon the inherent potentialities of the tumor but also upon the tissue into which it is growing. At the present time, the characteristics employed in the grading of the gynecological tumors are based on tissue and not on cellular relationships. Therefore, the grading of invasive tumors such as cervical tumors is not entirely satisfactory because of the possible masking and subsequent modification of some of the tumor characteristics by the normal cervix which it must invade.

No correlation with malignancy is apparent from the results given in Table 3. The range of Q0, 's in air for the Grade I tumors is from 0.6 to 3.1, while corresponding values for Grade III cervical tumors is 0.4-3.2. Similarly, the lactic acid production and comparable determinations in oxygen (not given in tables) did not give values which can be correlated with malignancy.

Miscellaneous tumors.—The group of special tumors consists of diversified tissue, namely those tumors that could not be classified as gradable gynecological tumors. Included with the miscel-
laneous tumors are metastatic growths and certain uncommon ovarian tumors. The $Q_0$'s and lactic acid productions in air are given in Table 4. A gas phase of 100 per cent oxygen gave $Q_0$'s that were greater than those in air; the magnitude of the increase was approximately the same as that obtained with the other gynecological tumors.

The ratio of molecules of glucose fermented to those oxidized was also calculated for cervical tumors (Table 3). The average values for the Grades the human ovary. The characteristics chosen for this study were the oxygen uptake and lactic acid production. Both the $Q_0$ and $Q_{LA}$ values for the ovarian papillary serous tumors were higher in the more malignant tumors than they were in the benign tumors, thus showing correlation with malignancy. Similarly, the $Q_0$ values of pseudomucinous tumors could be correlated with the degree of malignancy. With the $Q_{LA}$ values of the pseudomucinous tumors, on the other hand, no correlation was apparent. In contrast with this correlation with malignancy of both the $Q_0$ and $Q_{LA}$ values of papillary serous tumors and the $Q_0$ of the pseudomucinous tumors, no correlation was obtained for either $Q_0$ or $Q_{LA}$ of the epidermoid carcinoma of the cervix. This behavior might have been predicted for cervical tumors because of their heterogeneity and the unsatisfactory criteria used at present for histological grading. The results obtained with miscellaneous tumors have shown that eleven out of seventeen tumors had $Q_0$ values of 1.1 to 1.9. That such a diversified group of tumors should exhibit a narrow range of $Q_0$ values is of particular interest and may reflect a convergence

### Table 2

<table>
<thead>
<tr>
<th>Grade and Tumor Number</th>
<th>$Q_0^*$</th>
<th>$Q_{0A}^*$</th>
<th>$Q_{LA}^*$</th>
<th>$Q_{0A}^*$</th>
<th>$Q_0^*$</th>
<th>$Q_{0A}^*$</th>
<th>$Q_{LA}^*$</th>
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<td>Benign</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>0.1</td>
</tr>
<tr>
<td>36</td>
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</tr>
<tr>
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<td>1.3</td>
</tr>
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</table>

I and II cervical tumors were within the range obtained for comparable grades of papillary serous tumors. The Grade III cervical tumors, however, showed a large drop in this ratio, e.g., average 8.0 for Grade III tumors as compared with 21.1 and 6.1 for Grades II and I, respectively. Under these circumstances it is difficult to say whether or not these results for cervical tumors showed any correlation with malignancy.

### Discussion

Numerous metabolic characteristics have been employed to distinguish normal from tumor tissues. The present paper is concerned with distinguishing between benign and malignant tumors of...
of many types of tumors to a common biochemical pattern.

Since the histological sections of ovarian papillary serous tumors have shown that Grade III tumors have a higher content of epithelium than the corresponding benign tumors, it may be preferable finding is, of course, in agreement with the obser-

TABLE 3

OXYGEN CONSUMPTION AND LACTIC ACID PRODUCTION OF HUMAN EPIDERMOID CARCINOMA OF CERVIX

<table>
<thead>
<tr>
<th>GRADE AND TUMOR NUMBER</th>
<th>QO₂*</th>
<th>QO₂†</th>
<th>QLA‡</th>
<th>QLA§</th>
<th>MOLES GLUCOSE FERMENTED</th>
<th>MOLES GLUCOSE OXIDIZED</th>
<th>RATIO OF MOLES GLUCOSE FERMENTED TO MOLES GLUCOSE OXIDIZED</th>
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<tbody>
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* See footnotes, Table 1.
† t ➷ ➷ ➷ ➷ ➷ ➷
‡ t ➷ ➷ ➷ ➷ ➷ ➷
§ t ➷ ➷ ➷ ➷ ➷ ➷

Plus (+) indicates irradiation, the time of which is unknown. Minus (—) indicates no irradiation.

...vations of Warburg and others (3, 6, 7, 9, 11, 14—17). It would be expected also that this ratio would be smaller in a gas phase of 100 per cent oxygen than in air, since aerobic processes would be stimulated and lactic acid production decreased in the presence of oxygen. Out of 25 tumors studied in both gas phases, twenty tumors had lower ratios in oxygen than in air. No explanation is offered for the behavior of the remaining five tumors.
The pioneering studies of Warburg (14) disclosed increased glycolysis for tumor as compared with normal tissues. With the histologically graded human ovarian papillary serous tumors, similar behavior was observed. Comparing the malignant with the benign tumors it was found that the aerobic lactic acid production in the presence of glucose was about 8 times greater for malignant than for benign tumors. Similar results were obtained in comparable QL production experiments with a gas phase of 100 per cent oxygen. The lactic acid production in nitrogen was 3-4 times greater than that observed in oxygen or air. Apparently, therefore, the QL can be used not only to distinguish some normal from tumor tissue, but also benign from malignant human papillary serous tumors.

In addition to lactic acid production, there are other characteristics that have been used to distinguish normal from tumor tissues. Among these are respiratory quotient (R.Q.), Meyerhof Quotient, Absolute Pasteur Effect, and Fermentation Excess (6). Since most of these biochemical characteristics have been determined with tissues of animal origin, it was of interest to study the behavior of a few spontaneous human tumors.

Dickens and Simer (4, 5) found that some tumors with high Q00 had R.Q.'s (0.82–0.98) which

### TABLE 4

**OXYGEN CONSUMPTION AND LACTIC ACID PRODUCTION OF HUMAN MISCELLANEOUS TUMORS**

<table>
<thead>
<tr>
<th>Tumor No.</th>
<th>Type of tumor</th>
<th>Q00</th>
<th>Q01</th>
<th>QL4</th>
<th>Q00</th>
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</thead>
<tbody>
<tr>
<td>80</td>
<td>Omental metastasis</td>
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<td></td>
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<tr>
<td>81</td>
<td>Omental metastasis</td>
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<td>1.0</td>
<td>2.5</td>
<td>11.0</td>
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<tr>
<td>82</td>
<td>Vaginal and rectal metastasis</td>
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</tr>
<tr>
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<td>Omental metastasis</td>
<td>1.1</td>
<td>0.6</td>
<td>0.2</td>
<td>3.3</td>
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</table>

**Miscellaneous ovarian tumors**

<table>
<thead>
<tr>
<th>Tumor No.</th>
<th>Type of tumor</th>
<th>Q00</th>
<th>Q01</th>
<th>QL4</th>
<th>Q00</th>
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</thead>
<tbody>
<tr>
<td>84</td>
<td>Cystadenofibroma (benign)</td>
<td>0.5</td>
<td>0.2</td>
<td>8.8</td>
<td>21.6</td>
</tr>
<tr>
<td>85</td>
<td>Cystadenofibroma (benign)</td>
<td>0.5</td>
<td>0.3</td>
<td>0.5</td>
<td>3.6</td>
</tr>
<tr>
<td>86</td>
<td>Benign teratoma with predominant struma ovarii</td>
<td>1.3</td>
<td>0.7</td>
<td>0.0</td>
<td>2.5</td>
</tr>
<tr>
<td>87</td>
<td>Papillary adenocarcinoma struma ovarii</td>
<td>1.9</td>
<td>1.9</td>
<td>1.9</td>
<td>12.2</td>
</tr>
<tr>
<td>88</td>
<td>Adenocarcinoma in endometrioma ovary</td>
<td>0.6</td>
<td>0.5</td>
<td></td>
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</tr>
<tr>
<td>89</td>
<td>Clear cell carcinoma of ovary</td>
<td>0.9</td>
<td>0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90</td>
<td>Primary ovarian adenocarcinoma—not gradable</td>
<td>2.7</td>
<td>2.6</td>
<td>0.5</td>
<td>10.0</td>
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**Dysontogenetic tumors of ovary**

<table>
<thead>
<tr>
<th>Tumor No.</th>
<th>Type of tumor</th>
<th>Q00</th>
<th>Q01</th>
<th>QL4</th>
<th>Q00</th>
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</thead>
<tbody>
<tr>
<td>91</td>
<td>Thecoma (benign)</td>
<td>1.8</td>
<td>1.5</td>
<td>0.8</td>
<td>7.9</td>
</tr>
<tr>
<td>92</td>
<td>Thecoma (benign)</td>
<td>1.1</td>
<td>1.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>93</td>
<td>Thecoma (malignant)</td>
<td>1.5</td>
<td>1.2</td>
<td>0.0</td>
<td>2.0</td>
</tr>
<tr>
<td>94</td>
<td>Thecoma (granulosa-cell tumor)</td>
<td>1.9</td>
<td>1.9</td>
<td>0.0</td>
<td>18.9</td>
</tr>
<tr>
<td>95</td>
<td>Omental metastasis of primary granulosa-cell tumor</td>
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<td>1.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>96</td>
<td>Dysgerminoma</td>
<td>0.9</td>
<td>1.0</td>
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</tr>
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</table>

* See footnotes, Table 1.
† = " " " "
‡ = " " " "
§ = " " " "

### TABLE 5

**THE MEYERHOF QUOTIENT, ABSOLUTE PASTEUR EFFECT, FERMENTATION EXCESS, AND RESPIRATORY QUOTIENT OF SOME GYNECOLOGICAL TUMORS**

<table>
<thead>
<tr>
<th>Tumor No.</th>
<th>Type of tumor</th>
<th>Meyerhof quotient*</th>
<th>Pasteur effect†</th>
<th>Fermentation excess‡</th>
<th>R.Q.§</th>
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<td>III</td>
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<td>Epidermoid carcinoma of the cervix</td>
<td>II</td>
<td>5.3</td>
<td>2.3</td>
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</tr>
<tr>
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<td>Epidermoid carcinoma of the cervix</td>
<td>II</td>
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<tr>
<td>94</td>
<td>Epidermoid carcinoma of the cervix</td>
<td>II</td>
<td>7.2</td>
<td>3.6</td>
<td>0.6</td>
</tr>
<tr>
<td>95</td>
<td>Epidermoid carcinoma of the cervix</td>
<td>none</td>
<td>56.0</td>
<td>9.8</td>
<td>10.0</td>
</tr>
<tr>
<td>96</td>
<td>Thecoma</td>
<td>none</td>
<td>7.2</td>
<td>4.3</td>
<td>0.0</td>
</tr>
<tr>
<td>97</td>
<td>Vaginal and rectal metastasis ovarian carcinoma</td>
<td>none</td>
<td>40.8</td>
<td>21.6</td>
<td>19.0</td>
</tr>
<tr>
<td>98</td>
<td>Omental metastasis ovarian carcinoma</td>
<td>none</td>
<td>40.5</td>
<td>13.5</td>
<td>11.6</td>
</tr>
</tbody>
</table>

* Meyerhof Oxidation Quotient \( \frac{Q_{01} - Q_{00}}{Q_{00}} \).
† Absolute Pasteur Effect \( Q_{01} - Q_{00} \).
‡ Fermentation Excess \( Q_{01} - 2Q_{00} \).
§ Respiratory Quotient \( \frac{Q_{00}}{Q_{00}} \).
are below values obtained with total carbohydrate oxidation. A few such determinations with human gynecological tumors (Table 5) have revealed R.Q values of 0.50–0.81, in spite of a high aerobic lactic acid production.

With one exception, No. 82, the Absolute Pasteur Effect$^1$ and the Fermentation Excess$^2$ of some human tumors (Table 5) fall within the ranges usually obtained for tumor tissue, e.g., the range of 8 to 15 for Pasteur Effect and $-5$ to $+25$ for Fermentation Excess. The exception to this behavior, tumor No. 82, when compared with the other human tumors has a high Absolute Pasteur Effect (21.6), a high Q$^{2}$ but a low Q$^{0}$. It appears surprising that this tumor, which can produce large amounts of lactic acid anaerobically, fails to accumulate significant amounts of lactic acid in the presence of oxygen. The three tumors which exhibited a high Meyerhof Quotient$^3$ (Nos. 61, 82, and 88) all have Q$^{2}$ values above 10 with Q$^{0}$ values of about 1.0. The Q$^{2}$ in these cases are low, as mentioned above for tumor No. 82, but the most outstanding feature of these tumors is the high anaerobic lactic acid production.

It is apparent from the preceding discussion that the results obtained for the lactic acid production, Respiratory Quotient, Absolute Pasteur Effect, and, in some cases, the Meyerhof Quotient of human gynecological tumors conform to the general pattern found with animal tumors.

**SUMMARY**

1. The Q$^{0}$’s and Q$^{2}$’s of a number of human ovarian papillary serous tumors have been determined and found to correlate apparently with histologically determined grades of malignancy. Similar correlation was found for the oxygen consumption of human ovarian pseudomucinous tumors. According to the present system of histological grading for cervical tumors, on the other hand, no correlation was evident for either the Q$^{0}$’s or Q$^{2}$’s. The Q$^{0}$, and Q$^{2}$, values of a group of miscellaneous gynecological tumors are also reported.

2. Calculation of the molecules of glucose fermentation/molecules of glucose oxidized for ovarian papillary serous tumors has provided some correlation with malignancy; higher values indicating more glycolysis were obtained for the malignant tumors. This calculation eliminated the error in the metabolic results caused by variation in the epithelium to stroma ratio. Inconclusive results were obtained by this calculation on pseudomucinous and cervical tumors.

3. Ovarian papillary serous tumors and a small group of other gynecological tumors were found to have Respiratory Quotients, Lactic Acid Production, Pasteur Effect, and Fermentation Excess which were within the range of values obtained for animal tumors. A few discrepancies were obtained with the values of the Meyerhof Quotient.

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Chemical Characteristics and Varying Degrees of Malignancy in Tumors of the Human Ovary: I. Oxygen Consumption and Lactic Acid Production

Helena de Roeth


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