

Comparison of the β -Glucuronidase Activity of Normal, Tumor, and Lymph Node Tissues of Surgical Patients¹

WILLIAM H. FISHMAN and A. J. ANLYAN

*Departments of Surgery and Biochemistry,
University of Chicago*

The physiological role of β -glucuronidase is believed to be that of "metabolic conjugation" (2), especially of the estrogenic hormones. In many animal experiments (2, 4) β -glucuronidase has been shown to be elevated specifically in response to estrogen injection. The excretion of large amounts of steroid glu-

At this time, confirmatory data are presented as well as some new observations on the β -glucuronidase content of human tissues (Table 1). The presence of relatively large amounts of β -glucuronidase in the involved lymph nodes of cancerous patients is reported for the first time (Table 2).

The main observations were as follows: Whereas minimal differences from normal were seen in benign fibroadenoma and gynecomastia of the breast, striking elevations were observed in carcinoma, fibrosarcoma, and in the proliferated lactating breast. In the uterus, the normal endometrium was high in glucuronidase. Carcinoma of the uterus contained more enzyme than did uninvolved uterine tissue. Uterine fibroid was relatively low in activity. In carcinoma of the gastrointestinal

TABLE 1

Patient†	Pathological diagnosis		Glucuronidase units*	
	Lesion	Organ	Tissue	
			Tumor	Normal
K	Benign fibroadenoma	Breast	393	325
C	Gynecomastia	"	267	—
W	"	"	96	—
L	Post-partum death	"	—	1,050
C	Carcinoma	"	890	140
R	" , scirrhous and medullary	"	1,930	62
M	Carcinoma	"	945	—
M	"	"	900	94
D	Fibrosarcoma	"	1,230	145
N	Fibroid	Uterus	405	—
L	Myometrium at parturition	"	—	844
V	Atrophy	"	—	365
H	Recurrent carcinoma	"	884	199
N	Normal endometrium	"	—	2,020
N	Adenocarcinoma	Colon	1,320	1,480
G	"	"	2,770	1,628
O	"	"	1,360	1,760
V	"	Rectum	900	1,930
M	"	Colon	5,250	2,490
N	Lipoma	"	126	1,311
L	Adenocarcinoma	Stomach	3,180	940
K	"	Cardia	1,510	750
B	"	"	2,180	650
B	Benign islet cell adenoma	Pancreas	960	600
E	Carcinoma, scirrhous	"	172	326
L	Post-partum death	"	—	1,045
N	Adenocarcinoma, metastatic	Liver	1,650	2,980
J	" , recurrent (ovary) mucinous	Abdominal wall	1,410	—
C	Carcinoma of ovary, recurrent	"	2,740	554 (mesentery)

* One unit is defined as 1 μ g. of phenolphthalein liberated from phenolphthalein mono- β -glucuronide per hour at 38° from 1 gram of moist tissue under standard conditions (3).

† Patients previously studied (1) have been included for purposes of comparison.

curonides in pregnancy, an observation many times confirmed by others, was accompanied by elevations in blood glucuronidase activity (1). It was also reported (1) that malignant neoplasms of the breast and gastrointestinal tract contained more β -glucuronidase activity than did the corresponding uninvolved tissue.

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TABLE 2

Patient	Pathological diagnosis	Site of tumor	Site of lymph node	Glucuronidase units	
	Lesion			Involved node	Uninvolved node
C	Carcinoma	Breast	Axilla	2,740	694
T	Malignant melanoma	Index finger	"	2,532	680
W	Carcinoma	Prostate	Cervical region	6,700	—
B	"	Colon	Mesentery	1,590	206

tract, elevations in glucuronidase occurred in the cardioesophagus, stomach, and less frequently in the colon. In tumors of the pancreas no change or a decrease in activity was observed. Adenocarcinoma, recurrent and metastatic to the abdomen, contained relatively large amounts of enzyme. Lymph nodes which have been removed from patients with cancer of the breast, colon, and prostate and with malignant melanoma contained excessive amounts of β -glucuronidase as compared with the corresponding uninvolved tissue.

The observation of the enhanced β -glucuronidase activity of lymph nodes involved by cancer seems particularly important. Here, the lymph nodes may be considered to be tissue cultures of cancer cells, and this is where the highest glucuronidase concentrations have been observed. The same is true for mesenteric recurrences of cancer.

Two important questions arise from these results. Is enhanced glucuronidase activity a characteristic of cancer cells? If so, what is the significance of this finding?

In considering the first question, a clear-cut answer at first would appear difficult in view of the results in carcinoma of the pancreas and in a few cases of adenocarcinoma of the colon. However, if the tumor is small and is surrounded by much fibrous tissue, differences in activity may be impossible to demonstrate. Also, the adenocarcinoma of the colon involves both mucosal and muscle elements, whereas the control tissue has been colon mucosa, which possesses high glucuronidase activity. Nevertheless, 11 of 14 of the primary neoplastic tissues, 4 of 4 metastases to lymph nodes, and 3 of 3 recurrences to abdominal wall and uterus contained increased glucuronidase activity. Accordingly, the view may be taken that elevated β -glucuronidase is probably a characteristic of malignant cells, although a high glucuronidase activity in a tissue does not necessarily imply malignant change.

The question of the significance of the presence of higher activities of β -glucuronidase in tumor tissues cannot be answered at this time. Studies of many other enzymes in tumor tissue have shown, in the majority of cases, a lowered activity as compared to the enzymic activity of normal tissues.

References

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Blood Plasma Ascorbic Acid Levels on Controlled Intakes of Ascorbic Acid

MARY L. DODDS and FLORENCE L. MACLEOD

*Agricultural Experiment Station,
University of Tennessee, Knoxville*

A survey of the ascorbic acid status of college students reported from the University of Tennessee in 1944 (1) indicated a limited relationship between the fasting blood plasma ascorbic acid level and the calculated intake of ascorbic acid the preceding day.

An outgrowth of this work was a series of studies, from 1942 to 1947, with subjects maintained on controlled intakes of ascorbic acid. Considerable data were accumulated on blood plasma ascorbic acid values on these intakes. Since the plasma ascorbic acid is often determined in population survey studies, a statement of these values, with their standard deviations, may aid in the interpretation of survey data and indicate the dietary intake of ascorbic acid in these populations.

The subjects were 41 young women in their early 20's who weighed 44-76 kg., with an average weight of 57 kg. The

TABLE 1

BLOOD PLASMA ASCORBIC ACID VALUES WITH STANDARD DEVIATIONS FOR 41 SUBJECTS (MEAN WEIGHT, 57 KG.)

Intake ascorbic acid (mg.)	Plasma ascorbic acid (mg./100 ml.)	Standard deviations (mg./100 ml.)	Range (mg./100 ml.)
32	0.48	± 0.137	0.34-0.62
57	0.72	± 0.210	0.51-0.93
82	0.93	± 0.196	0.74-1.13
107	1.05	± 0.170	0.88-1.22

fasting plasma ascorbic acid values given in Table 1 are 2-day and 6-day averages following 7- to 10-day adjustment periods at each level of intake. Fifty, 75, and 100 mg. were given daily as the synthetic vitamin. The diet contained an average of 7.1 mg. of reduced ascorbic acid. In the first experiments on 17 subjects, intakes were increased by intervals of 25 mg. Later, 24 subjects on the same intakes were studied, but with increasing and decreasing intervals of 25 and 50 mg. The changes in the time and intake schedules as the study progressed were the result of statistical evaluation of existing data and were made to enlarge the scope of the findings.

A 25-mg. ascorbic acid intake for 6 days or 2 weeks preceded the experimental periods. The blood plasma ascorbic acid

values of subjects at this intake decreased or were barely maintained. Adjustment to intake is not claimed for this preliminary period, and the plasma ascorbic acid value given for it is undoubtedly high. A curve through the three experimental values places this plasma level at approximately 0.43 mg. of ascorbic acid/100 ml.

Overlapping of values at the intervals studied becomes more pronounced at the 82- and 107-mg. intakes, perhaps indicating adequacy at the lower level for some subjects. The standard deviation determines the range within which two-thirds of the plasma ascorbic acid values of subjects maintained on the corresponding intake will fall. The wide range in the plasma ascorbic acid values at each of the three levels of controlled intake indicates that any estimation of the vitamin intake of a population based on a plasma ascorbic acid survey cannot be narrowly defined.

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Humidity and Tolerance to Low Barometric Pressure

NORMAN E. PHILLIPS, PAUL A. SAXON, and
FREEMAN H. QUIMBY

*Department of Zoology,
University of Maryland, College Park*

During experiments in respiration at low pressure it became apparent that high humidities increase the ability of Swiss Albino mice to withstand reduced pressure.

Young male mice ranging in weight from 20 to 30 grams are placed in a small low-pressure chamber, and the pressure is reduced at the rate of 1 cm./minute. The behavior of the animals is closely observed, and the pressure at which respiration stops is noted. Provision is made for controlling the humidity of the air entering the chamber. Tests have been run at 22°, 10°, 0°, -10°, and -20° C. At each combination of temperature and humidity 10 or more animals have been tested.

At all temperatures used, air of 100 per cent humidity increases, in comparison to dry air, the tolerance of the mice to pressure reduction. This effect is most noticeable at -10° C., at which temperature mice in dry air die at an average pressure of 418 mm. Hg (15,500 feet simulated altitude). In air of 100 per cent humidity death occurs at 180 mm. Hg (35,000 feet). At other temperatures the beneficial effect of humidity is somewhat less, but still appreciable. The optimum conditions for survival of these animals are 0° C. and 100 per cent humidity, in which state the pressure is reduced to about 40 mm. Hg before death ensues.

Humidities of 65 and 90 per cent have been employed, but the results indicate that these humidities do not improve the tolerance of mice above that afforded by dry air.

Experiments to determine the effects of humidity on the tolerance of human subjects to reduced pressures, and low temperatures, are in progress. Also, the study on mice is being extended to include the effect of humidity on other respiratory factors.