tional disturbances in pyridoxine deficient organs.

Summary. Total blood and plasma volumes measured by use of radioactive iodinated serum albumin ($RI^{131}SA$) were not altered from normal by chronic pyridoxine deficiency in male and female rats. The average total blood volume as determined by this radioisotopic technic is somewhat higher than values obtained elsewhere by the Evans blue dye method.

Organ weight changes have been measured and compared in pyridoxine deficient, desoxypyridoxine treated, and pyridoxine treated rats. Wet and dry weights of the liver, kidney, adrenal, spleen and testes of the deficient animals were greater compared to the pyridoxine treated rats. Administration of the antivitamin, desoxypyridoxine, to pyridoxine deficient rats not only increased the apparent hypertrophy of these organs, but also accentuated the marked atrophy of thymus associated with pyridoxine deficiency.

1. Hsu, J. M., Davis, R. L., Chow, B. F., *J. Biol. Chem.,* 1958, v230, 889.

2. Hartsook, E. W., Hershberger, T. V., *J. Nutrition,* 1960, v72, 297.

3. Stebbins, R. B., *Am. J. Physiol.,* 1951, v116, 538.

4. Brown, M. L., Pike, R. L., *J. Nutrition,* 1961, v71, 191.

5. Agnew, L. R. C., PROC. SOC. EXP. BIOL. AND MED., 1955, v90, 452.

6. Olsen, N. S., Martindale, W. E., *J. Nutrition,* 1954, v53, 329.

7. Butler, L. C., Morgan, A. F., PROC. SOC. EXP. BIOL. AND MED., 1954, v85, 441.

Received October 30, 1961. P.S.E.B.M., 1962, v109.

Monoamine Oxidase Activity in Human Tissues and Intestinal Biopsy Specimens. (27160)

ROBERT J. LEVINE AND ALBERT SJOERDSMA
Experimental Therapeutics Branch, National Heart Institute, Bethesda, Md.

Knowledge of the tissue distribution of monoamine oxidase (MAO) has been of value in determining the sites of inactivation for amines such as 5-hydroxytryptamine and norepinephrine. Such information is also helpful in attempting to explain the pharmacologic actions of MAO-inhibiting drugs. It is more desirable to consider human amine metabolism in terms of MAO levels in human rather than animal tissues because wide variation between species in the distribution of this enzyme are known to occur(1). Since previous studies(1) of this enzyme in humans have been limited to only 6 tissues, a more complete survey of MAO in human tissue was undertaken and is reported here.

Heretofore, estimation of MAO activity in living humans was dependent on indirect methods of evaluation such as the assay of one of its substrates, *e.g.,* tryptamine, in the urine(2). The recent development of a highly sensitive method for assay of MAO in tissues(3) permits direct measurements of enzyme activity in small tissue specimens. The results of applying this technic to biopsies of intestinal mucosa from normal subjects are presented.

Materials and methods. Specimens of tissue were obtained within 8 hours after death from each of 7 patients. Of these, 5, ages 22 to 60, died following unsuccessful cardiac surgery; one, age 31 died of a convulsive disorder; and one, age 2, died of congenital hydrocephalus. None had received hormones or drugs known to alter MAO activity. Tissue specimens were frozen promptly until time of assay, within 48 hours. Tissues with gross abnormalities in appearance were not studied. Utilization of postmortem material for determining distribution of MAO was considered valid because the activity of this enzyme is quite stable even at room temperature for 24 hours(1). Furthermore, sympathetic ganglia obtained at surgery have MAO activity in the same range as those obtained at autopsy (3).

TABLE I. Monoamine Oxidase Activity of Various Human Tissues Obtained at Autopsy.

Tissue†	Range*	Avg*
Liver (5)	16 - 32	25
Kidney (4)	11 - 27	15
Heart (4)	7.4 - 15	10
Lung (4)	6.0 - 11	8.1
Thyroid (4)	4.8 - 7.2	6.4
Adrenal (5)	5.2 - 7.2	6.3
Pancreas (5)	1.6 - 8.6	4.9
Sympathetic ganglion (4)	3.3 - 6.1	4.4
Cerebral cortex (4)	3.3 - 4.9	4.0
Pituitary (3)	1.5 - 1.8	1.6
Spleen (4)	.60- 1.5	1.0
Skeletal muscle (4)	.61- .89	.69
Testis (3)	.46- .55	.49

* Values expressed as micromoles of indoleacetic acid formed per g of tissue per hr of incubation.
† No. of specimens assayed in parentheses.

Jejunal mucosa was obtained from each of 13 normal subjects by the capsule biopsy technic of Crosby(4). Specimens weighing 22 to 90 mg (average 38 mg) were obtained in this fashion and only rarely, due to mechanical failure, was no suitable specimen obtained. Specimens were promptly removed from the capsule, debrided of tissue which appeared nonviable, weighed and then either assayed promptly or frozen for no more than 24 hours before they were assayed.

All assays for MAO activity were done by a previously described method(3), using tryptamine as a substrate and measuring the formation of indoleacetic acid (IAA).

Results. MAO activity of various human tissues obtained at autopsy is recorded in Table I. High levels were present in liver, heart, kidney, and lung and very low levels in testis and skeletal muscle. The activities of the other tissues assayed were in an intermediate range. It was also attempted to study the gastrointestinal mucosa but due to very rapid postmortem deterioration of this tissue the results were extremely erratic. No MAO acivity was detected in blood cells or plasma of normal subjects.

The results of assay of MAO in biopsies of jejunal mucosa are recorded in Table II. The range in the entire series was 32.3 to 46.2 micromoles of IAA formed per gram of tissue per hour with a standard deviation of 3.1 μm/g/hr. Assays on repeat biopsies in the same individual produced results differing by an average of only 2.2 μm/g/hr and not exceeding 6.0 μm/g/hr.

Discussion. The MAO activity of the tissues of various species has been classified as high, moderate and very low or absent(1). In general, the activity of human tissue may be classified similarly. The most notable exception is that in the heart, which has high MAO activity in humans but very low activity in most other species. MAO activity is absent from the blood of humans but has been detected in the plasma of some other mammals(5).

Davison(1) reviewed previous data on distribution of MAO activity in human brain, heart, lung, muscle, liver and kidney using tyramine as a substrate. Our findings are similar except that almost no activity was found in skeletal muscle while he reported activity comparable to that present in the cerebral cortex. In addition, we have extended the survey to include other tissues in which the effects of MAO-inhibiting drugs may be observed. For example, these drugs have been found to block transmission at sympathetic ganglia in cats(6) and to inhibit the amine induced stimulation of beef pituitary glucose oxidation(7). Since MAO activity of human pituitary is far less than that of beef pituitary, one would predict lesser effects

TABLE II. Monoamine Oxidase Activity of Jejunal Mucosa of Normal Subjects.

Age	Sex	No. of biopsies	MAO activity*
19	♂	3	36.8-42.8
20	♀	3	38.8-44.2
27	♂	2	40.0-41.4
19	♀	3	32.3-33.9
19	♂	3	37.3-39.7
26	♂	2	41.9-43.4
20	♀	2	37.4-38.2
20	♀	2	38.0-39.4
32	♀	2	43.1-44.5
21	♀	2	41.7-42.8
20	♀	2	40.0-42.8
21	♀	2	44.5-46.2
20	♀	2	40.5-41.1
	Range:		32.3-46.2
	Avg of individual means:		40.4 ± 3.1 (S.D.)

* Values expressed as μmoles of indoleacetic acid formed/g of tissue/hr of incubation.

of MAO inhibition on the metabolism of glucose by the human gland.

The finding that MAO activity of intestinal mucosa exceeds greatly that of any other tissue was not anticipated. In subsequent studies of the rat and the guinea pig, however, we found that a similar relationship exists. It is unfortunate that postmortem specimens of intestinal mucosa are unsuitable for study since this makes comparisons with the activities of other tissues within single individuals impossible.

The jejunal biopsy technic of Crosby makes it possible to obtain tissue specimens for assay of MAO activity frequently with minimal discomfort and essentially no risk to the subject. The use of a direct assay technic obviates sources of error inherent in indirect approaches such as measurement of urinary amines. The range of values for MAO activity in jejunal mucosa is sufficiently small so that it is not difficult to identify variations from normal when they occur in disease states or under the influence of various drugs. The very small range of variation in a single subject on different days makes studies involving the use of an individual as his own control most useful for evaluating the effect of a drug on MAO activity. We have had occasion to perform biopsies in hypertensive subjects as many as 10 times with all assays of MAO activity falling within a range of 12%. Preliminary observations on lowering of enzyme activity by MAO inhibiting drugs or in hyperthyroid states have shown this to be a very reliable and satisfactory technic for direct detection of spontaneous and induced variations of MAO activity.

Summary. The distribution of monoamine oxidase activity in human tissues was surveyed. The significance of this distribution and the differences between humans and various animal species were discussed. Direct assay of MAO activity in specimens of jejunal mucosa obtained from human subjects by peroral biopsy was shown to be feasible. In a series of normal subjects studied in this fashion the range of variation is sufficiently narrow to make this a useful procedure for detection of spontaneous and induced variations of MAO activity.

1. Davison, A. N., *Physiol. Rev.,* 1958, v38, 729.
2. Sjoerdsma, A., Oates, J. A., Zaltzman, P., Udenfriend, S., *J. Pharmacol. and Exp. Therap.,* 1959, v126, 217.
3. Lovenberg, W., Levine, R. J., Sjoerdsma, A., *J. Pharmacol. and Exp. Therap.,* 1962, v135, 7.
4. Smith, R. B. W., Sprinz, H., Crosby, W. H., Sullivan, B. H., *Am. J. Med.,* 1958, v25, 391.
5. Blaschko, H., Friedman, P. J., Hawes, R., Nilsson, K., *J. Physiol.,* 1959, v145, 384.
6. Gertner, S. B., *Nature,* 1959, v183, 750.
7. Barondes, S. H., Johnson, P., Field, J. B., *Clin. Res.,* 1961, v9, 175.

Received October 31, 1961. P.S.E.B.M., 1962, v109.

Serum Enzyme Studies in Muscular Dystrophy. III. Serum Malic Dehydrogenase, 5-Nucleotidase and Adenosinetriphosphatase.* (27161)

SUDHIR R. CHOWDHURY, CARL M. PEARSON, WILLIAM W. FOWLER, JR. AND WENDELL H. GRIFFITH
Departments of Physiological Chemistry and Medicine, and Division of Neurology, University of California School of Medicine, Los Angeles

The assay of serum enzymes has become an established diagnostic procedure in clinical medicine. Commonly assayed enzymes, such as glutamic oxalacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), lactic dehydrogenase (LDH), and aldolase, are widely distributed in mammalian tissues and are found in variable and, usually, in high concentrations in the liver and in cardiac and skeletal muscle. In normal subjects these enzymes are almost exclusively confined within the body cells where

* This study was supported by a grant from the Muscular Dystrophy Associations of America.