THE OXYGEN CONSUMPTION OF DIFFERENT STRAINS OF MICE

by

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OXYGEN CONSUMPTION OF DIFFERENT STRAINS OF MICE

In comparing mice of several strains, differences were found in adult body weight, thyroid weight and asphyxiation time (Krueger, Mason and Bogart). A sex influence on asphyxiation time was also noted; in two strains females had longer survival times during asphyxiation, and in another two strains the females had shorter survival times. Asphyxiation time had been presumed to be an indicator of the general metabolic oxygen requirement and hence, to be an index of thyroxin level or thyroid activity of the mice, since in man, basal levels of oxygen consumption are highly correlated with levels of thyroid activity (1, p. 814-823). Hence, it seemed advisable to study oxygen consumption of mice of different strains to see if the oxygen consumption ran parallel to the asphyxiation time. The purpose of this thesis is to compare the oxygen consumption of males and of females of two different strains of mice. Further, some differences between the two strains in the alteration of oxygen consumption after thiouracil will be noted. The interrelations between oxygen consumption, asphyxiation time, and thyroid weights will be also discussed.

LITERATURE REVIEW

The literature on metabolism in general, and on oxygen consumption in particular, is very extensive. An attempt will be made in this thesis to cover mainly papers in the literature concerned with oxygen consumption in mice, the effects of thiouracil and related compounds on mice, and the course of recovery of mice from thiouracil.

Oxygen consumption: In Table 1 are given data on oxygen consumption of mice as found in the literature. The mice used ranged in weight from 8.0 to 57.0 grams. Oxygen consumed per mouse per hour ranged from 8.3 to 130 ml. Oxygen consumed per gram of mouse per hour ranged from 1.0 to 6.8 ml. Perusal of the data reported in individual papers indicated wide individual variability of the mice. It is obvious from the data of Hart (7) that the ambient temperature was of importance.

Mørsh (15) determined the carbon dioxide produced by mice using a gas-chain method fro separation of carbon dioxide and water. By using a respriatory quotient of 0.8, the carbon dioxide production values were converted (at OSC) to oxygen consumption data and recorded in table 1. Benedict and Lee (3) and Benedict (2) reported their data as heat production. Average heat production ranged from 110 to 195 calories per kg per hour for white, obese, dwarf and wild mice. These data were converted into ml of oxygen on the basis that 1 ml of oxygen was equivalent to 4.8 calories. Various devices for measuring oxygen consumption directly were used by the other authors quoted in table 1.

Table 1. Oxygen Consumption of Mice as Reported in Literature

Authors	Weight Grams	Oxygen Consumed Per mouse ml/hr	Oxygen Consumed ml/gr/hr	Jar T °C	Remarks
MØRSH (1929)	8.0	43.5	6.80	23	From CO_2 production
	14.5	72.9	4.69	23	
	18.0	78.2	5.39	23	
Benedict & Lee			1.0-2.0		From heat production
(1933)	21	30.0	1.42		White mice
	57	23.8	1.08		Obese mice
	8	8.3	1.00		Dwarf mice
	19	28.1	1.50		Wild mice
Davis & Van Dyke	24.0-28.2	34-81	1.4-3.3	28	Fasting mice: Boston
(1933)	25.2 av.	42.1	1.67		
	26.0-32.3	41-50	1.5-1.7	28	Fasting mice: Chicago
	28.6 av.	45.9	1.60		
Benedict (1938)	20	34	1.7		From heat production
Stadie & Haggard			1.7		Under nembutal
(1946)			2.6		After nembutal
Hart (1950)	26.7 av.	130	4.87	15	Read from graph
		110	4.12	20	
		80	3.00	25	
		60	2.25	30	

Table 1 (continued). Oxygen Consumption of Mice as Reported in Literature

Authors	Weight Grams	Oxygen Consumed Per Mouse ml/hr	Oxygen Consumed ml/gr/hr	Jar T °C	Remarks
Maclagan & Sheahan (1950)			2.1-2.4	27	Groups of eight mice
Clark & Otis (1952)			3.2	23	
Marshall & Mayer (1954)	21.5 av.	77.1	3.6		Non-obese
	42.6	101.3	2.4		Obese

Davis and Van Dyke (6) studied the oxygen consumption of seven mice in Boston, Mass. and in Chicago, Ill. The observations were made 17-24 hours after the last access to food. The chamber used was of eight liters capacity. Readings were taken at 5 minute intervals. Average oxygen consumptions per gram of mouse per hour were 1.67 ml at Boston and 1.60 ml at Chicago and 42.1 ml per mouse per hour at Boston, but 45.9 ml per mouse per hour at Chicago. The mice were older and weighed an average of 3.4 grams more at Chicago. The behavior of a mouse during any one determination was characterized by states of quiet, sleep, and activity, the proportions of which varied from determination to determination.

Hart (7) studied the interrelationships between metabolic rate and environmental temperature in resting mice. The mice were run in groups of four. Two to four 10-minute readings were obtained, averaged and reported as oxygen consumption per mouse. Oxygen consumption was high at the lower environmental temperatures and decreased as temperature was increased.

MacLagan and Sheahan (12) were concerned with the quantitative assay of thyroxine compounds and noted that quantitative assays were not usually obtained with single animals on account of individual variation in oxygen consumption. They therefore determined oxygen consumption on groups of eight mice at a time. They reported values of 2.14 - 2.35 ml of oxygen consumed per gram per hour at 27°C jar temperature. They record that the measurement of oxygen consumption

in their hands had proved disappointing for the assay of thyroid activity and that more than eight animals per group might be necessary for a satisfactory assay. Thus Maclagan and Sheahan emphasized individual variability.

Marshall and Mayer (13) studied the oxygen consumption of normal mice and of mice made obese by the intraperitoneal injections of gold thioglucose. The mice treated with gold thioglucose ate more, were less active, and consumed more oxygen than the normal mice. When reduced to a unit weight basis, however, the obese mice used less oxygen per gram of mouse than did the normal mice. Benedict and Lee (3) found lower oxygen consumption in obese than in non-obese mice on both the per mouse and per gram basis. Moreover, the oxygen consumed was higher in the data of Marshall and Mayer (13) for both obese and non-obese mice than in the data of Benedict and Lee.

Thus the literature disclosed that the oxygen consumption of mice is very variable, and that among the factors known and presumed to play a role in levels of oxygen consumption are the dietary history of the mouse (especially the time relationship between last access to food and the oxygen consumption), body weight, degree of activity, presence of sleep, the ambient temperature and the effects of drugs such as thyroxin, nembutal and gold thioglucose. No evidence of either an increase or a decrease in oxygen consumption following thiourea, thiouracil or related compounds in normal mice was found in the literature. For mice with body weights similar and under environmental

temperatures comparable to those used at Oregon State College, oxygen consumption varied from 34 to 80 ml per mouse per hour and from 1.7 to 5.4 ml per gram per hour.

Asphyxiation Time: Various authors have used survival time in a closed chamber to study relative rates of metabolism. Because different authors used chambers of different sizes their data are usually not directly comparable.

Smith, Emmens and Parker (18) reported that the survival time of mice held in sealed 1-quart jars was decreased by treatment with iodinated casein, and the relationship between dose and survival time was linear. Males were less variable than females in their response. Females had longer survival times normally and after thyroxin than did males. Burris, Bogart and Krueger (4) reported that survival times of female mice, when the mice were treated with beef cattle thyroid macerated subcutaneously, were greater than the survival times of male mice. However, Krueger, Mason and Bogart (9) reported asphyxiation times for males and females of O strain mice as 26.0 and 23.1 minutes, while weights were 31.7 and 31.9 grams, respectively; here male mice had the longer survival times. The difference may depend upon the fact that the female mice used by Krueger, Mason and Bogart had borne litters, while virgin females were used by Burris, Bogart and Krueger; the same strain of mice was involved, but some modification may have occurred over five or more years.

Smith (1948) indicated that the survival time of mice was prolonged by treatment with thiourea. Effective doses were 0.1 and 0.4 mg subcutaneously daily for 5-10 days and 0.025 mg daily for 10 or 20 days. Administered orally, concentrations of 0.01, 0.04 and 0.16 percent in drinking water for 5 or 10 days were effective. Large doses of thiourea caused a high mortality and morbidity rate and also shortened the survival time (17).

Effects of Thiouracil in Mice: Sheahan, Wilkinson and MacLagan (16) found that inhibitory analogues of thyroxin (n - Alkyl 3:5-Diiodo-4-Hydroxybenzoates) when given alone to normal mice induced no significant alteration in metabolism. However, the inhibitory analogues of thyroxin decreased the high oxygen consumption of mice treated with thyroxin. The depression of oxygen consumption in mice, previously treated with thyroxin, was difficult to explain. But the authors stated that it is well known that a depression of metabolism is not easy to achieve in normal mice even with drugs of the thiourea type. No data or references were given to support the thiourea statement.

Wilkinson, Sheahan and MacLagan (21) noted that Barker had found 2:4 diiodophenoxyacetic acid active as a thyroxin inhibitor in rats, but this compound was ineffective in the hands of Wilkinson and his coworkers as a thyroxin inhibitor in mice. Thyroxin activity and inhibition were followed by studying oxygen consumption.

Hurst and Turner (8) studied the thyroid secretion rate in mice and its relation to various physiological processes. They

found that the incorporation of 0.05 or 0.1 percent thiouracil into the feed for a two week period did not significantly increase the weight of the thyroid gland of the mature mouse. The addition of 0.2 percent thiouracil to the feed, however, did increase thyroid weight significantly during a two week period.

The literature thus discloses that survival time of mice was increased after prolonged treatment with thiourea. The literature also indicates that some thyroxin inhibitors will lower rates of oxygen consumption rendered high in mice by previous treatment with thyroxin; but direct depression of oxygen consumption, by thyroxin inhibitors, thiourea, or thiouracil, is difficult to obtain. Compounds effective in depressing oxygen consumption in rats are not necessarily effective in mice. While thiouracil does not depress the oxygen consumption of mice, thiouracil has a goitrogenic effect in mice.

MATERIALS AND METHODS

Previous studies (Krueger, Mason and Bogart, 1956) indicated that there were sex and strain differences in body weight, thyroid weight and asphyxiation times of mice. To adequately compare several strains of mice was too imposing a problem and hence only two of the strains of mice were chosen for study. The two groups of mice selected for study had clearly different genetic backgrounds. (One represented an inbred line and the other a crossbred group. To facilitate discussion both groups hereafter will generally be referred to as strains.)

Oxygen consumption data were collected on mice under routine conditions and during and after the administration of thiouracil. Subsequently the mice were asphyxiated and the time required for asphyxiation noted. Autopsies were performed immediately and the thyroids were excised and weighed. A statement is required for the description of the mice, the experimental procedure, and the method for determining oxygen consumption.

Mice: Many strains of mice have been developed since January, 1955, in the Small Animal Laboratory at Oregon State College. Two strains of these mice were selected for this experiment. For one of the strains chosen there were originally about 5 females and 2 males in the Laboratory of the Dairy and Animal Husbandry Department. These were expended into the O strain or strain 1. The original

source is not definitely known; but the strain had been maintained for some time in small numbers and with rather rigid selection for large body size, litter size and general high vigor.

Another strain, the A strain or strain 11, had been maintained by the Entomology Laboratory of the U.S.D.A. at Corvallis, Oregon for sometime after being originally imported from an indefinite source in California. A third group of mice, at the Oregon State College Veterinary Diagnostic Laboratory, was degenerating in body size, litter size and general vigor. This group of mice had been imported from California, and Possibly the more healthy appearing mice had been selected for experimental work, leaving the poor ones for breeding stock. These mice were designated the V strain or strain 6. A fourth strain of mice from the Cutter Laboratories at Berkeley, California, were added as the C strain or strain 16. In this strain fertility was extremely low.

One particular mating of the V strain produced an exceedingly small and uniform litter. This litter was saved, mated together, selected for small body size, and developed into the M strain or strain 24. By crossing of the A,V,O,C strains together a new group called the D strain or strain 20 was developed.

A female of strain D (A,V,O,C) was accidently mated to a wild mouse. The F_1 litter was saved, mated together and also mated to strain M. The F_2 mice and the back cross mice (to strain M)

were mated together and also backcrossed to the F_1 parents, and the generation produced by these matings provided the foundation for strain W or strain 25. The W and O strains were selected for this experiment.

Mice of the W Strain: Twenty males of the W strain were individually mated with twenty females of the W strain on August 6, 1957. The males were removed August 20, 1957. Eighteen of the twenty females had litters between August 26 and August 28, and a 19th female gave birth to a litter on August 30, 1957. In the nineteen litters 141 mice were born and 113 were surviving after 20 days; of these, 65 were males and 48 were females. One male and one female were randomly selected from each litter for maintenance of the W strain. It was subsequently possible to pick one male and one female (randomly selected within the litter and within sex as far as required or possible) from 17 litters. The three additional males and females were then randomly selected from the remaining mice to provide twenty males and twenty females.

Thus, 40 mice, twenty males and twenty females, were available for oxygen consumption studies from the mildly inbred W strain and were essentially the same age, with the oldest varying only three days from the youngest.

Mice of the O Strain: Nineteen males of the O strain were individually mated with nineteen females of the O strain on August 6, 1957. The males were removed August 20, 1957. Fourteen of the nineteen females had litters between August 26 and August 29, and

a 15th female gave birth to a litter on August 30, 1957. In the fifteen litters, 117 mice were born and 82 were surviving after 21 days; of these, 48 were males and 34 were females. One male and one female were randomly selected from each litter for maintenance of the O strain. One additional male and one additional female were then picked randomly as far as required or possible from each of the 15 litters. An additional five mice of each sex were selected randomly from the remaining pool of surviving mice to give 20 males and 20 females.

Thus 40 mice, twenty males and twenty females, were available for oxygen consumption studies from the inbred strain O. These mice were essentially of the same age, the oldest being only four days older than the youngest.

Orientation experiments indicated that there would be a considerable lapse in days in obtaining oxygen consumption data on eighty mice. As the main interest was in strain and sex differences, and as the mice were of essentially the same age, the eighty mice were divided into twenty quartets of four mice each, with one O male, one O female, one W male and one W female randomly allotted to each quartet.

Experimental Procedure: Except during mating and lactation all mice were individually caged in the same racks in the Oregon State College Small Animal Laboratory. The temperature of the laboratory was thermostatically regulated at 72-76° F. The mice were fed a

commercial pelleted mouse ration (Rockland). Food and water were available ad libitum. The young were kept with their mothers until weaning.

For determination of oxygen consumption the mice were moved from the Small Animal Laboratory to Withycombe Hall, room 207, which was free from contamination with the excess carbon dioxide present in some rooms where dry ice was being used to freeze semen. Control levels of oxygen consumption were obtained between November 8 and November 30, 1957. Oxygen consumptions were usually run for two quartets (8 mice) each day when practical. One to five days after the oxygen consumption determination the quartets of mice were placed on a diet containing 0.1% thiouracil. The thiouracil and the pellets of the regular ration were ground together every two to three days in order to keep the thiouracil incorporated in the diet as much as possible. Sometimes some of the thiouracil obviously separated from the diet as an impure white powder. The quartets of mice were kept on thiouracil 45 to 56 days. Oxygen consumption was determined as feasible on various quartets over the periods representing the interval of 25 to 55 days on thiouracil. In general, oxygen consumption was determined three times for each quartet during exposure to thiouracil.

Nine of the twenty quartets were left on thiouracil for 51 to 54 days and were then killed by suffocation in one half pint sealed Mason jar. Oxygen consumption was determined for each quartet on

the day prior to asphyxiation. Following death the thyroids were dissected out immediately and weighed on a Roller-Smith torsion balance.

The remaining eleven quartets were kept on thiouracil 45 to 56 days and then returned to the pelleted ration without thiouracil. During the period of recovery, which was varied from 13 to 34 days, oxygen consumption was run twice on some quartets and once on others. On the day following the last oxygen consumption determination the mice were killed by asphyxiation in half pint sealed Mason jars. Asphyxiation time was determined and the thyroids were immediately excised and weighed.

Four of the eighty mice were lost during the experiment and one died. Thus some quartets were represented by only three survivors. The data were statistically treated by analysis of variance according to methods outlined in Li (11).

Determination of Oxygen Consumption: For the determination of oxygen consumption the mice were placed in a one-quart Mason jar, with a capacity of 964 ml and fitted with a screw cap into which a sensitive thermometer and a glass T tube were inserted. The thermometer and T tube were sheathed in rubber tubing to make sure the container was airtight (10, 20). One side of the T tube was connected with rubber tubing to a 10 ml graduated pipette and the other side to a 4 ml syringe (see Figure 1). The graduated pipette extended parallel to the table. A small wire cylinder about 2.5 inches wide by 5 inches long, 16 mesh to the inch, was constructed to hold the mouse. Two hundred grams of soda lime (Baker 4-8 mesh),

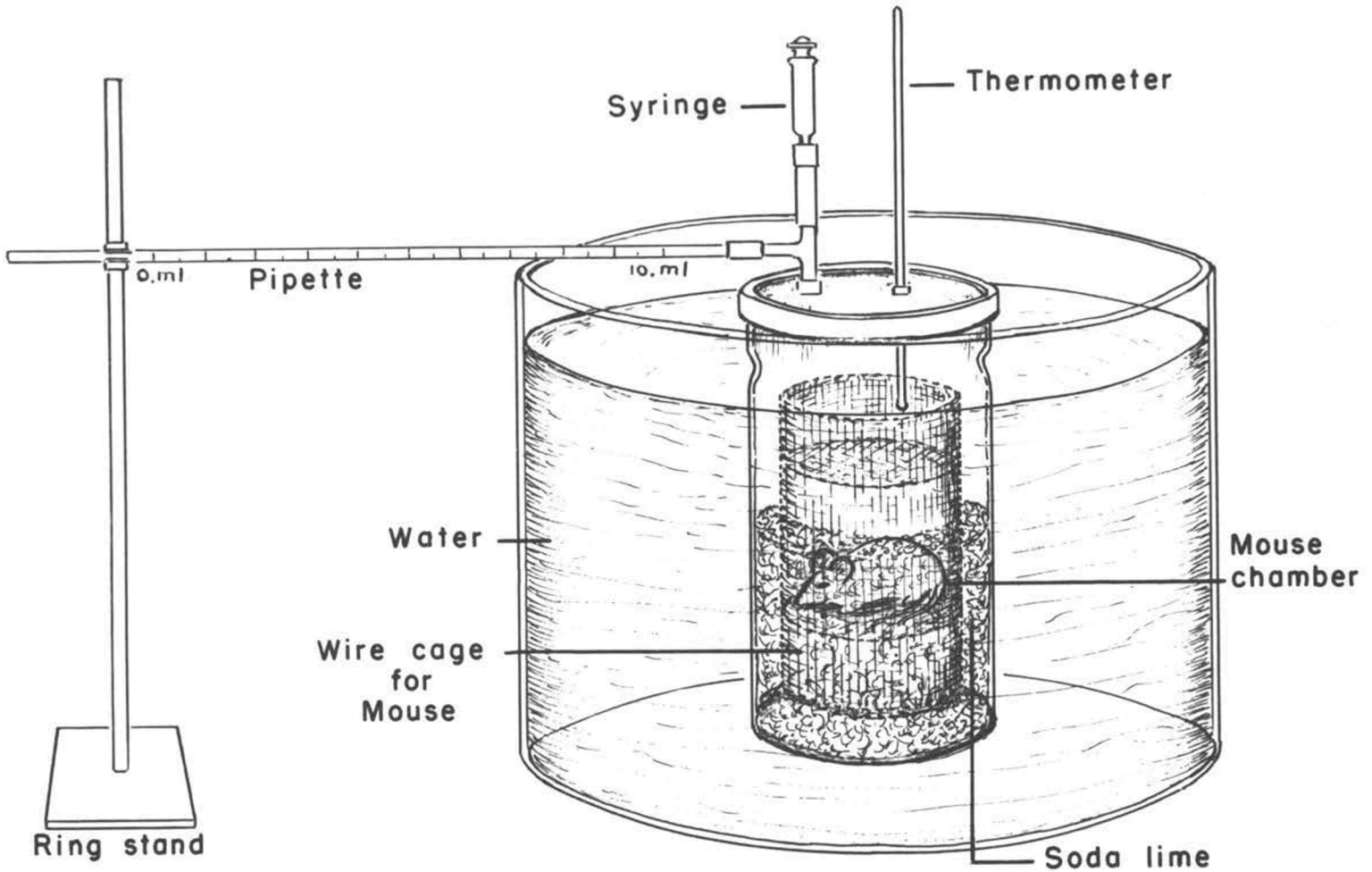

Figure 1

Apparatus for Oxygen Consumption

with a volume of 114 ml as determined by water displacement, was placed in the jar. The mouse, in the wire cylinder was placed in the jar, and the jar was sealed with the screw cap. The jar was then placed in a water bath. Some ten minutes later, after steady state conditions had been approximated, the end of the pipette was sealed with a water film from a detergent solution.

As carbon dioxide was absorbed by the soda lime, the rate at which oxygen was consumed by the animal in the jar was indicated by the movement of the detergent film through the calibrated pipette.

The mice had approximate volumes of 20 to 39 ml. Thus, approximately 820 ml (volume of jar less volume of soda lime less volume of mice; 964-114-30 ml) of air were available for the mouse. The temperature of the water bath and that inside the jar was read every 2-3 minutes. The barometric pressure was read before starting the measurement, and at the end of the measurement of the time required to consume 10 ml of oxygen. In general the time required to consume 10 ml of oxygen was determined three times for each mouse. Sometimes breaking of the water film precluded obtaining three full 10 ml consumption periods.

The time for consuming 10 ml of oxygen was converted into ml of oxygen consumed per mouse and ml of oxygen consumed per gram of mouse.

Calculation of Oxygen Consumption: The volumes of oxygen consumed were reduced to 0°C and 760 mm. Hg. by the relationship:

$$V\,(STP) = V\,(RTP) \times \frac{\text{Barometric pressure}}{760} \times \frac{273}{\text{Jar Temperature}} \qquad (1)$$

where V (STP) is the volume at standard conditions and V (RTP) is the volume at temperature and pressure of measurement.

If the jar temperature was unaltered during the time required to use 10 ml of oxygen, the 10 ml were reduced to volume under standard conditions by filling in formula (1) as follows:

$$V\,(STP) = 10 \times \frac{\text{Barometric pressure}}{760} \times \frac{273}{\text{Jar Temperature}} \qquad (2)$$

If the temperature within the jar increased, the apparent oxygen consumption of 10 ml has to be increased by $\frac{1}{273}$ of the volume of air available to the mouse for each degree increase in temperature. The volume of 820 ml would increase $\frac{820}{273}$ or 3.0 ml for each degree increase in jar temperature. A volume of 0.3 ml would have to be added to apparent oxygen consumption for each 0.1 degree change in temperature. Likewise, for a decrease in temperature of -0.1°C, a volume of 0.3 ml would have to be subtracted from the apparent oxygen consumption. Thus the volume to be reduced to standard condition is actually 10 ml at RTP if the jar temperature did not change and 10 ml + 3 dT where the jar temperature change dT is positive if the temperature increased, and negative if the jar temperature decreased.

The volume of oxygen consumed per mouse per hour was given by the volume consumed multiplied by 60 and divided by the consumption time in minutes. The volume per mouse per hour divided by the weight of the mouse gave the oxygen consumed per gram of mouse per hour. The following examples illustrate the procedures followed:

Example: 1. No Change in Jar Temperature.

Time	0' min	4'10"
Pipette Reading	10 ml	0 ml
Barometer	762 mm Hg	762 mm Hg
Jar Temperature	26°C	26°C
Weight of Mouse	21 g	21 g

10 ml of oxygen measured at room temperature and pressure, were used in 4'10". The volume at 0° and 760 mm of Hg is given by

$$V(STP) = 10 \times \frac{273}{273 + 26} \times \frac{762}{760} = 9.154 \text{ ml.}$$

$\frac{273}{273 + 26}$ is the temperature correction and $\frac{762}{760}$ is the barometric correction.

Four minutes and ten seconds equals 4.167 minutes. 9.154 divided by 4.167 gives the oxygen consumption per minute; further multiplication by 60 gives the oxygen consumed per hour

9.154 ml/4.167 min = 2.197 ml per mouse per min

(9.154 ml/4.167 min)x60 = 131.81 ml per mouse per hour

131.81 ml/hr + 21 g = 6.28 ml per gram of mouse per hour

Example: 2. Increase in Jar Temperature

Time	0'	4'31"
Pipette Reading	10 ml	0 ml
Barometer	763 mm Hg	763 mm Hg
Jar Temperature	26.2	26.4
Weight of Mouse	22 g	22 g

The volume of the system was reduced 10 ml, but the increase in temperature of the jar expended the volume of air. An amount of oxygen equivalent to this expansion was used as well as the 10 ml indicated by the shift in the pipette reading. Thus $\underline{2 \times 0.3}$ or 0.6 ml must be added to the 10 ml loss noted by the burette. Hence, 10.6 ml of oxygen, measured at 26.4°C and 763 mm Hg pressure were used in 4'31". The volume used under standard conditions was:

$$V(STP) = V(RTP) \times \frac{273}{273 + 26.4} \times \frac{763}{760}$$

$$= 10.6 \times 0.9118 \times 1.0039 = 9.70 \text{ ml}$$

Four minutes and 31 seconds equal 4.157 minutes.

9.70 ml/4.517 min = 2.147 ml/min per mouse

2.147 ml/min x 60 min = 128.8 ml per mouse per hour

128.8 ml/hr ÷ 22.0 g = 5.85 ml per gram per hour

Example: 3. Decrease in Jar Temperature

Time	0'	4'31"
Pipette Reading	10 ml	0 ml
Barometer	763 mm Hg	763 mm Hg
Jar Temperature	26.2	26.0
Weight of Mouse	22 g	22 g

The volume of the system was reduced 10 ml, but the decrease in temperature of the jar contracted the volume of air. An amount of oxygen equivalent to this contraction was not used. Thus $\underline{2 \times 0.3}$ or 0.6 ml must be subtracted from the 10 ml less noted by the burette. Hence, 9.4 ml of oxygen, measured at 26.0°C and 763 mm Hg pressure were used in 4'31". The volume used under standard conditions was:

$$V(STP) = V(RTP) \times \frac{273}{273 + 26.0} \times \frac{763}{760}$$

$$= 9.4 \times 0.913 \times 1.0039 = 8.616$$

Four minutes and 31 seconds equal 4.517 minutes.

8.616 ml/4.517 min = 1.907 ml/min per mouse

1.907 ml/min x 60 min = 114.4 ml per mouse per hour

114.4 ml/hr $\div$ 22.0 = 5.20 ml per gram per hour

EXPERIMENTAL FINDINGS

Summaries of the data collected are gathered in tables 2-5. These data require discussion from the point of view of sex and strain differences in oxygen consumption and body weight prior to any treatment with thiouracil; the effect of thiouracil on oxygen consumption; sex and strain differences in the effect of thiouracil; sex and strain differences in recovery from thiouracil; and sex and strain differences in asphyxiation time and thyroid weights. The interrelations between oxygen consumption and asphyxiation time will also be discussed.

Oxygen Consumption and Body Weight Prior to Thiouracil Treatment: There were statistically (P less than 0.01) significant sex and strain differences in both body weight and oxygen consumption per mouse per hour (table 2). Males weighed more than females and consumed more oxygen per hour. O mice had greater body weights and consumed more oxygen per hour than W mice. However, the sex and strain differences in oxygen consumption ceased to be statistically significant when oxygen consumption was expressed on a per gram per hour basis. (Standard deviations for oxygen consumption per mouse per hour and per gram of mouse per hour respectively were 24.5 and 0.89 ml respectively.)

Effects of Thiouracil: It had initially been anticipated, on the basis of commonly accepted generalities, that thiouracil would depress oxygen consumption (Turner, p. 77-118), and that an effect would be evident within four weeks. The data initially collected

were times-to-use-10 ml-of-oxygen at room temperature and pressure. Calculations to oxygen per mouse per hour and per gram per hour were not made until the entire experiment had been completed. As no decreases in oxygen-consumption-times were evident after four weeks on thiouracil, the thiouracil feeding was continued until some decreases in oxygen consumption-times were evident at about 50 days on thiouracil.

When the data were finally calculated and tabulated (table 3), it was noted that there were statistically significant differences due to strain in the effects of thiouracil on oxygen consumed per mouse or per gram of mouse per hour (P less than 0.01).

In table 3 are recorded average values of oxygen consumed per mouse per hour, of the oxygen consumed per gram of mouse per hour, and of body weights. The first and second sections of the table give data on oxygen consumption rates and the third and fourth sections data on body weight and changes in body weight. The body weight data and the data on change in body weight show some inconsistencies due to sampling variation. The data tabulated under body weight give averages for the group measured and comparison with the initial column are subject to sampling error. The data listed under change in body weight take into consideration the individual initial non-thiouracil data and the individual data obtained while the mice were on thiouracil. Weight data based on averages of all mice used will obviously vary from weight data where identical mice are compared.

The fifth section of table 3 gives the number of mice available for each average. The first column contains control data obtained prior to the administration of thiouracil and subsequent columns data obtained during the administration of thiouracil.

An analysis of variance for the data of table 3 is given in table 3 A.

Thiouracil and Body Weight. The sex and strain differences in body weight, which had been observed prior to thiouracil, were still in existence after 50-55 days on thiouracil. The O mice weighed more than the W mice and the males weighed more than the females.

Most of the mice gained weight during the time they were on thiouracil. There were no sex or strain differences in gain but there was an interaction of sex x strain, the O males gaining more than O females and the W females gaining more than the W males. This implies that both sex and strain play interacting (presumably act in opposite directions) roles in weight changes on thiouracil.

Thiouracil and Oxygen Consumption per Unit of Body Weight. While the data collected directly by the experiment were oxygen consumption rates per mouse, the control data prior to thiouracil indicated that oxygen consumption per mouse was rather clearly the product of oxygen consumption per unit of body weight multiplied by the body weight. Thus oxygen consumption per unit of weight can be considered a simpler characteristic than oxygen consumption per mouse and it is logical to discuss oxygen consumption per unit of body weight before discussing oxygen consumption per mouse.

Table 2

Standard Data on Oxygen Consumption and Body Weight of Male and Female Mice of the W and O Crosses

		O Male	O Female	W Male	W Female
Weight: (g)	Mean:	30.70	26.06	27.51	22.38
	Range:	24.7-37.2	21.2-30.3	23.1-31.9	9.9-28.9
Oxygen: (ml/hr)	Mean:	146.4	127.3	134.4	110.2
	Range:	91-215	88-167	78-174	79-140
Oxygen: (ml/g/hr	Mean:	4.78	4.89	4.90	4.97
	Range:	3.2-6.2	3.6-5.7	2.7-6.7	4.0-6.0

Analysis of Variance

Variate	Degrees of Freedom	Mean Squares: Weight	Oxygen Consumption ml/hr	Oxygen Consumption ml/g/hr
Sex	1	477.0203**	9376.62**	0.1624
Strain	1	235.8128**	4218.06**	0.2000
Sex x Strain	1	1.2127	128.77	0.0102
Error	74	9.9866	593.69	0.7948

** Significant at the 1% level of probability.

Table 3

Oxygen Consumption of Mice on Thiouracil

Days on Thiouracil	Control	25-30	30-35	35-40	40-45	45-50	50-55
				Oxygen consumption per mouse per hour			
W males	135	143	139	126	130	123	120
W females	110	131	119	104	113	100	101
O males	146	158	151	152	143	144	137
O females	127	126	145	150	138	139	133
				Oxygen consumption per gram per hour			
W males	4.90	5.11	4.74	4.61	4.36	4.41	4.32
W females	4.97	5.74	5.37	4.34	4.89	4.24	4.03
O males	4.77	5.44	5.00	4.74	4.83	4.59	4.49
O females	4.89	4.74	5.07	5.60	4.98	5.15	4.96
				Body weight: grams			
W males	27.5	28.3	29.3	27.2	29.1	27.6	28.4
W females	22.4	23.0	22.1	24.3	23.6	24.0	25.1
O males	30.7	29.3	30.5	32.0	31.4	32.4	31.4
O females	26.1	26.5	28.8	26.7	27.8	27.1	26.1
				Change in body weight on Thiouracil (grams)			
W males	-	-.17	-.16	+.44	1.14	0.74	1.27
W females	-	-.06	2.08	0.76	1.87	1.94	2.02
O males	-	0.33	0.89	0.93	1.96	0.76	1.19
O females	-	-1.15	1.04	0.55	1.30	1.09	1.02
				Number of mice			
W males	20	5	6	9	10	11	15
W females	19	5	6	8	11	10	14
O males	19	5	6	9	9	12	14
O females	20	5	6	9	10	12	16

Table 3A
Analysis of Variance for Data Collected During Administration of Thiouracil

	Degrees of Freedom	Mean Squares		
		Gain in Weight	Oxygen Consumption ml/mouse/hr	Oxygen Consumption ml/g/hr
Time	5	1.76**	156.071*	0.345**
Sex	1	0.67	709.209**	0.143
Strain	1	0.34	1865.296**	0.497**
Sex x time	5	0.63	110.532	0.2418**
Strain x time	5	0.09	144.746*	0.187*
Sex x strain	1	2.97*	68.494	0.0144
Sex x strain x time	5	0.18	56.858	0.094
Error	198	0.55	61.142	0.077

There was no statistically significant sex or strain difference in oxygen consumption per unit of body weight prior to thiouracil. W males, W females, and O males showed decreases in oxygen consumption with time on thiouracil. O females showed a statistically significant increase in oxygen consumption (P less than 0.05) 35-40 days on thiouracil, but there was no statistically significant residual increase in oxygen consumption per gram of mouse at 50-55 days on thiouracil as compared with prethiouracil data.

Initially males and females were similar, but after 50-55 days on thiouracil the O males were using oxygen at a significantly lower rate per gram of mouse than the O females. At 50-55 days there was no statistically significant difference between W males and W females, but the W females had the lower oxygen consumptions. Hence thiouracil either induced or emphasized a sex difference in the O mice and possibly in the W mice.

Oxygen consumption per gram of mouse per hour decreased on thiouracil in the W strain; but any decrease noted in the O strain was not statistically significant. Thiouracil may even have increased the oxygen consumption of O females over the period from the 25th and 50th day. Thus thiouracil either induced or emphasized a strain difference between the W and O mice in oxygen consumption per unit of body weight.

Thiouracil and Oxygen Consumption per Mouse. During the administration of thiouracil, the average values of oxygen consumed per mouse per hour varied widely but most of the differences noted were not

statistically significant. The dearth of statistical significance may reflect the fact that no observations were made during the first 25 days on thiouracil and only groups of 5 or 6 mice were studied over the intervals 25-30 and 30-35 days.

The sex and strain differences in oxygen consumption per mouse per hour which had previously been observed were still in existence while the mice were on thiouracil. The W mice used less oxygen than the O mice and the females less than the males. In addition the oxygen consumption per mouse per hour decreased with time, but this was entirely due to the W strain.

At the end of 50-55 days on thiouracil the males still had higher oxygen consumption rates than the females, and the O mice had higher oxygen consumption rates than the W mice. Thiouracil emphasized the differences in oxygen consumption between the strains but decreased the difference between the sexes. The decrease in sex difference in oxygen consumption of the males (W females decreased slightly and O females increased). For the strain effect thiouracil decreased the oxygen consumption of the least active group (the W) and for the sex effect thiouracil decreased the oxygen consumption of the more active group (the males).

A statistically significant decrease in oxygen consumption at the end of 50-55 days on thiouracil was retained only in the W males (P less than 0.05)

The analysis of variance (Table 3A) indicates that both oxygen consumption per mouse and per gram of mouse per hour decreased with time. Per mouse there was a significant difference between males and

not females, but per gram of mouse per hour there was no difference. Thus weight played an important part in the difference established in oxygen consumption per mouse.

While no statistically significant difference between males and females was established with respect to oxygen consumption per gram of mouse, sex played a significant role in alterations of oxygen consumption rates by thiouracil. Males and females did not react similarly to thiouracil. With increased time on thiouracil, the differential effects of thiouracil in males and females tended to cancel one another. This implies that all the effects of thiouracil were not linear with time.

RECOVERY FROM THIOURACIL: Pertinent data on recovery from thiouracil are given in tables 4 and 5. Table 5 also includes summarizing data for control, thiouracil and recovery periods.

Average data on oxygen consumption are given in the upper two sections of table 4, and data on body weight in the third section, data on gain in the fourth section. The fifth section gives the number of observations available per cell for oxygen consumption and body weight data. An analysis of variance is given in table 4A. The first column gives average oxygen consumption and body weight data for the period prior to the administration of thiouracil, the second and third columns give data obtained from the mice 50-55 days after the administration of thiouracil started but still on thiouracil, and the last three columns give average data for 1-7, 13-19, and 25-33 days of recovery from thiouracil. The second column gives an average

value for all mice available in a given category, and the third column gives the average value for the mice selected to survive and recover from thiouracil. As the mice were killed 13-34 days after thiouracil, the last three columns are derived from sub groups of animals represented in column 3. The section on body weight contains groups averages, while the data on gain are derived from comparisons of weight differences within specific animals.

Body Weight During Recovery from Thiouracil: During the administration of thiouracil all mice gained in body weight. After 50-55 days on thiouracil the mice were divided into two groups, one to be sacrificed while still on thiouracil, and the other to be allowed to recover from thiouracil for 13-45 days and then sacrificed. The division into groups was accompanied by a slight alteration of means (table 5). During 25-33 days of recovery from thiouracil, W males gained 5.2 grams and O males gained 4.9 grams; W females and O females did not show statistically significant weight changes. Thus males of either strain gained markedly while the females did not show statistically significant gains.

Oxygen Consumption per Gram During Recovery from Thiouracil: It is possible that oxygen consumption per gram of mouse increased during the first week after cessation of thiouracil but insufficient data are available for a statistical statement. In the O mice there was a statistically significant early increase in oxygen consumption per gram during the first week of recovery from thiouracil.

If all the data on recovery from thiouracil are considered without taking time after thiouracil into consideration, and for the net effect of recovery over 25-33 days, the O and W females showed statistically significant increases in oxygen consumption per gram of mouse during recovery from thiouracil, while the O and W males did not develop statistically significant alterations in oxygen consumption per gram of mouse.

Thus there was a significant sex difference but no significant strain difference in oxygen consumption rates per gram during recovery from thiouracil as compared with oxygen consumption rates after 50-55 days of thiouracil treatment.

On comparing the pre-thiouracil control data with final recovery data 25-33 days after cessation of thiouracil it can be noted that the O females showed a statistically significant residual increase in oxygen consumption while W males, W females and O males did not retain statistically significant alterations in oxygen consumption per gram of mouse.

Oxygen Consumption per Mouse During Recovery from Thiouracil. Oxygen consumption per mouse per hour increased to a statistically significant extent during recovery from thiouracil as compared with data collected after 50-55 days on thiouracil. But no statistically significant sex or strain differences were apparent. Males showed slight increases in oxygen consumption per gram and extensive increases in body weight during thiouracil, while females showed marked increases in oxygen consumption per gram and only slight weight changes.

Thus the sex differences in gain and in oxygen consumption per gram during recovery from thiouracil were partially obliterated when combined into oxygen consumption per mouse.

Oxygen consumption per mouse per hour was slightly higher (P less than 0.05) at the end of recovery from thiouracil than prior to thiouracil treatment. This was mainly the effect of the increase in body weight.

Thiouracil and Thyroid Weight: In table 5 and 5A are given summarizing data on body weights, thyroid weights, asphyxiation times and oxygen consumption. Control (prethiouracil) data as not directly available for thyroid weights and asphyxiation times. However, average data for the O strain have been published in the literature (9). O strain males had asphyxiation times of 26.0 minutes and females 23.1 minutes. At body weights of 31.7 and 31.9 grams respectively, thyroid weights were 2.4 and 4.1 mg respectively. The data have been incorporated in table 5 and are placed in parentheses. The data in parentheses are not directly comparable to the data of this thesis, as they were collected more than a year ago, and hence, several generations earlier. Further, the females were non-virgin as compared to virgin females used for this thesis.

Thiouracil caused a great increase in thyroid size of both males and females of the O strain on the basis of data in the literature. Thus thiouracil was goitrogenic in the O mice even though there was no establishable decrease in oxygen consumption per mouse, and on a per gram of mouse basis, oxygen consumption did not change for O females

Table 4

Oxygen Consumption and Body Weight of Mice
Before, During and After Thiouracil

	Control	On Thiouracil 50-55 Days		Days After Cessation of Thiouracil 1-7	13-19	25-33
			Oxygen per mouse per hour			
		All	Selected			
W males	135	120	120	124	108	152
W females	110	101	101	117	139	114
O males	146	137	143	207	155	169
O females	127	133	132	143	143	154
			Oxygen per gram per hour			
W males	4.90	4.32	4.32	4.52	3.96	4.66
W females	4.97	4.03	3.96	4.71	5.18	4.90
O males	4.77	4.49	4.49	6.16	4.59	4.69
O females	4.89	4.96	4.80	5.87	5.24	5.53
			Body Weight			
W males	27.5	28.4	29.0	27.2	28.3	33.0
W females	22.4	25.1	24.9	24.8	26.9	23.1
O males	30.7	31.4	29.6	33.7	34.5	35.7
O females	26.1	26.1	24.4	26.6	27.8	27.8
			Gain in weight during recovery: grams			
W males				0.2	0.7	5.2
W females				1.1	0.5	1.3
O males				0.4	2.5	4.9
O females				0.5	1.2	1.2
			Number of mice			
W males	20	15	9	2	6	5
W females	19	14	9	2	3	7
O males	19	15	9	2	6	5
O females	20	15	9	2	6	5

Table 4A

Analysis of Variance of Data Collected On
Oxygen Consumption and Body Weight During Recovery from Thiouracil

	Degrees of Freedom	MEAN SQUARES		
		Gain in Weight	Oxygen Consumption	
			ml./mouse/hr.	ml./g./hr.
Sex	1	11.37**	1957	6.63**
Strain	1	2.00	757	1.54
Sex x strain	1	0.27	606	0.01
Error	48	0.88	862	1.09

Table 5

Body Weight, Thyroid Weight, Asphyxiation Time and Oxygen Consumption of W and O Mice Before, During and After the Administration of Thiouracil

	No.	W Males	W Females	O Males	O Females
Body Weight in grams					
Control (from literature)				(31.7)	(31.9)
Control (prethiouracil)	20	27.5	22.4	30.7	26.1
On Thiouracil (50-55 days)	9	29.0	24.9	29.6	24.4
Recovery (22-35 days)	5	33.0	23.1	35.7	27.8
Thyroid Weight in mg					
Control (from literature)				(2.4)	(4.1)
On Thiouracil (50-55 days)	9	11.2	13.9	12.0	11.1
Recovery (13-35 days)	11	9.7	6.7	7.6	6.3
Asphyxiation Time in minutes					
Control (from literature)				(26.0)	(23.1)
On Thiouracil (50-55 days)	9	29	34	23	31
Recovery (13-35 days)	11	25	32	20	28
Oxygen Consumption per Mouse per Hour in ml					
Control	20	135	110	146	127
On Thiouracil (50-55 days)	9	120	101	143	132
Recovery (22-35 days)	5	152	114	169	154
Oxygen Consumption per Gram per Hour in ml					
Control	20	4.90	4.97	4.77	4.89
On Thiouracil (50-55 days)	9	4.32	4.03	4.49	4.96
Recovery (22-35 days)	5	4.66	4.90	4.69	4.53

Table 5A

Analysis of Variance of Data Collected on Thyroid Weights and Asphyxiation Times.

	Degrees of Freedom	On Thiouracil	Recovery from Thiouracil	On Thiouracil	Recovery from Thiouracil
Sex	1	1.52	67.94**	1,289,779**	610,183**
Strain	1	0.07	30.12**	529,715**	1,642,680**
Sex x Strain	1	4.16	18.82**	67,934	7,870
Error	35	15.27	2.82	65,191	56,272

but decreased about 6 per cent in O males. The fact that thyroid size of W and O mice under the action of thiouracil was similar is highly indicative that thiouracil was also markedly goitrogenic in W mice.

No clear cut sex or strain difference was established for thyroid weights when the mice were under the action of thiouracil. However the average thyroid weight of the W females at 13.9 mg was significantly above that of the W males at 11.2 mg, of the O females at 11.7 mg and the O males at 12.0 mg (P less than 0.05; standard deviation of thyroid weights on thiouracil, 2.9 mg.).

Thyroid Weights on Recovery from Thiouracil. On recovery from thiouracil, thyroid weights decreased markedly and significantly but did not reach control (prethiouracil) levels, expected on the basis of data in the literature.

Statistically significant differences (P less than 0.01) due to sex, strain and sex x strain interaction were noted in the thyroid weights during recovery from thiouracil. At the end of the recovery period males had larger thyroids than did females and W mice had larger thyroids than did O mice. W females showed the greatest reduction in thyroid size and W males the least. In the W strain there was a marked sex difference in the thyroid weights on recovery; the sex difference was present but not prominent in the O strain.

Thiouracil and Asphyxiation Time. Marked differences were noted in asphyxiation times between sexes and between strains for mice under the action of thiouracil and also for mice recovering from the effects

of thiouracil. Sex x strain interaction for asphyxiation times was not statistically significant. (P less than 0.01; standard deviation of asphyxiation time, 5.5 minutes).

W mice on thiouracil and after recovery from thiouracil had longer asphyxiation times than O mice for both males and females. Females had markedly longer asphyxiation times than males.

Thiouracil presumably had caused an increase in asphyxiation time as was indicated by the decrease when the administration of thiouracil was stopped. Of the differences established between sexes, between strains and between thiouracil and recovery from thiouracil, the sex effect was of greatest magnitude and the thiouracil the least.

Asphyxiation times and oxygen consumption data do not run parallel. O males had much shorter asphyxiation times than O females, but average oxygen consumption rates per mouse were very similar for O males and O females. When asphyxiation times are plotted against corresponding oxygen consumptions, the points are highly scattered and no clear relations are apparent.

DISCUSSION

Oxygen Consumption: Our experience (data available but not included) agrees with that of other workers that oxygen consumption is altered depending upon the relationship between quiet, sleep and activity. Body weight, ambient temperature and the relationship to time of feeding are also factors contributing to variability. None of these factors can be adequately controlled without leading to difficulties in the interpretation of differences between strains of mice and between males and females.

Our data on oxygen consumption lie among the higher values reported in the literature. Roughly the overall oxygen consumption per gram of mouse per hour was 4.90 ml. Only Mørsh and Hart (15, 7) report oxygen consumptions of this magnitude. A possible reason why other workers have oxygen consumptions considerably lower than those reported here lies in the fact that our mice had feed continuously available, whereas in many laboratories the mice were kept from feed for 24-hours prior to the oxygen consumption determination. Because of the high metabolism of mice, this procedure was no adopted since it essentially requires measuring of oxygen consumption during starvation of the mice rather than merely on an empty stomach.

Extreme differences were noted by Benedict and Lee (3) with regard to the oxygen consumption of different types of mice, and their findings can be considered as consistent with those recorded here, in that we have also noted a strain difference.

While sex differences in asphyxiation times have been reported in the literature it is rather strange that no notations were found with respect to sex differences in oxygen consumption. A sex difference in oxygen consumption was noted in these experiments.

Asphyxiation Time: The data reported here on asphyxiation time is in agreement with that reported by Smith, Emmens and Parker (18) and by Burris, Bogart and Krueger (4) in that females have the longer survival times. They need not be considered as contradicting the observations of Krueger, Mason and Bogart (9) where male mice had the longer survival time. The females mice used in the study by Krueger,

Mason and Bogart (9) had borne litters, whereas the mice used in this series of experiments were virgin.

Effect of Thiouracil: The data here presented with respect to the action of thiouracil, where comparable, can be considered in agreement with the findings in the literature. Thiouracil caused a decrease in oxygen consumption only after prolonged administration at the dosage level of 0.1 per cent in the feed. As asphyxiation times were reduced on recovery from thiouracil, it may be presumed that thiouracil prolonged asphyxiation times.

Hurst and Turner (8) found no goitrogenic effect of 0.1 per cent thiouracil over a period of two weeks but obtained a definite goitrogenic effect when thiouracil was administered at the level of 0.2 per cent during a two week period. In these experiments thiouracil was given at the level of 0.1 per cent for six-eight weeks and hence does not contradict the observations of Hurst and Turner where 0.1 per cent thiouracil was administered for only two weeks.

Strain and Sex Similarities: There were a few characteristics for which the four groups (O males; O females; W males and W females) of mice could be considered as essentially similar. There were some consistent differences between the strains and there were some consistent differences between the sexes. Many of the differences were complex with an interaction between strain and sex.

All four groups of mice had similar rates of oxygen consumption per gram of mouse per hour. For all four groups the rate of oxygen consumption increased during recovery from thiouracil. For all four groups thiouracil was goitrogenic, and there was a decrease in thyroid

Size on recovery from thiouracil. For all there was a decrease in asphyxiation time on recovery from thiouracil.

Sex Similarities and Sex Differences: In addition to the sex similarities extending over both strains of mice there were similarities restricted to the O strain or the W strain. Males and females of the O strain were similar in that neither gained significantly in body weight while receiving thiouracil.

Males and females of the O strain were dissimilar in several respects. Males weighed more than females and had higher oxygen consumption rates per mouse per hour. Males showed no statistically significant change in oxygen consumption per mouse per hour or per gram per hour during the administration of thiouracil while oxygen consumption rates of O females increased. Males had lower asphyxiation times than females.

Males and females of the W strain were similar in several respects. These males and females had similar control levels of oxygen consumption per gram per hour. For both sexes oxygen consumption per gram of mouse per hour decreased during the administration of thiouracil. For both, oxygen consumption increased during recovery from thiouracil.

Males and females of the W strain were dissimilar in several respects. W males weighed more and had greater oxygen consumption rates than did W females. Oxygen consumption per mouse decreased in W males but did not change in females during the administration of thiouracil. Under the action of thiouracil, males had smaller thyroids than females, but following recovery from thiouracil males had the larger thyroids. There was less recovery in thyroid size in males than in females. Males

had smaller asphyxiation times than females.

Strain Similarities and Strain Differences: Simple similarities between strains were listed under strain and sex similarities. In addition there are some strain differences between males that do not exist, or are different, for females. Also there are strain differences between females, that do not exist, or are different, for males.

W males and O males were similar in several respects. Both had similar levels of oxygen consumption per gram per hour. Both W and O males gained during recovery from thiouracil. Oxygen consumption for both W and O males increased during recovery from thiouracil. W and O males had thyroids of similar size under the action of thiouracil. Thiouracil was goitrogenic in both W and O males. Asphyxiation time increased in both during recovery from thiouracil.

W males and O males were dissimilar in several respects. W males weighed less than O males. W males had lower levels of oxygen consumption per mouse than O males. W males showed a decrease in oxygen consumption under the action of thiouracil, while O males showed no change on both a per mouse and a per gram basis. W males had larger thyroids than O males following recovery from thiouracil. Recovery in thyroid size was less for W males than for O males. W males had longer asphyxiation times than O males.

W females and O females were similar in several respects. Both had similar control levels of oxygen consumption per gram per hour. Thiouracil was goitrogenic in W and O females. Thyroid weights of W and O females were similar during recovery from thiouracil.

W females and O females were dissimilar in several respects. W females weighed less than O females and had lower oxygen consumption rates. W females showed a decrease in oxygen consumption per gram per hour on thiouracil, while O females showed an increase in oxygen consumption per gram per hour. Oxygen consumption per mouse per hour on thiouracil did not change in W females, but increased in O females. W females on thiouracil had larger thyroids than O females. W females showed greater recovery in thyroid size than did O females. W females had longer asphyxiation times than O females.

Strain and Sex Interaction: Frequently differences between males and females were not quantitatively the same in W mice and in O mice. In other words, there were frequent sex and strain interactions. Interaction between sex and strain was noted for the effect of thiouracil on body weight, for thyroid size during recovery from thiouracil, and for the decrease in thyroid size on recovery from thiouracil.

Thiouracil, Oxygen Consumption and Asphyxiation Time: The data presented in this thesis can be considered as consistent with the literature with regard to control rates of oxygen consumption, with regard to the goitrogenic action of thiouracil in mice and the difficulty of decreasing the rate of oxygen consumption in mice by the administration of thiouracil. New information developed includes the establishment of strain and sex differences in oxygen consumption rates, asphyxiation times and the action of thiouracil.

While oxygen consumption per gram of mouse per hour was similar for males and females of the W and O strains, the items physiologically integrated into oxygen consumption must have been different as indicated

by the differential effects of thiouracil on oxygen consumption (increase in O females; decrease in W females, O males and O females).

The lack of correlation between asphyxiation times and oxygen consumption requires emphasizing the theoretical differences that may be involved. Asphyxiation includes oxygen utilization and the exposure to reduced oxygen pressure and to increased carbon dioxide pressure. Oxygen consumption might be different in mice disturbed by the asphyxiation procedure as compared with mice not disturbed by the procedure. It would be worth while designing experiments to evaluate separately these factors.

Sex, strain and thiouracil were factors in the differences noted in oxygen consumptions, asphyxiation times, and thyroid weights. These factors played the following relative roles with respect to the magnitudes of the differences:

Oxygen Consumption per mouse:	Strain > Sex > Thiouracil
Oxygen Consumption per gram:	Strain > Thiouracil > Sex
Asphyxiation Time:	Sex > Strain > Thiouracil
Thyroid Weight:	Thiouracil > Sex > Strain

Thus sex was the most potent factor of the three on asphyxiation time differences; strain was most potent for oxygen consumption differences and thiouracil for thyroid weight differences.

SUMMARY

Oxygen consumption rates, asphyxiation times, body weights and thyroid weights were studied on 20 mice each from W males, W females, O males and O females. The W and O mice represented different strains of

mice from the Oregon State College Small Animal Laboratory. The parents of the mice used were mated simultaneously in individual pairs. The mice used were all born over a period of four days.

Males weighed more than females and had a higher level of oxygen consumption per mouse. O mice had greater body weights and greater oxygen consumption rates per mouse than W mice. The sex and strain differences ceased to be statistically significant when oxygen consumption was expressed on a per gram per hour basis. Oxygen consumption per gram per hour for W males, W females, O males and O females respectively were 4.90, 4.97, 4.77 and 4.89 ml per gram per hour.

W females and O males showed no statistically significant differences in oxygen consumption on thiouracil as compared with respective control values. W males showed a decrease in oxygen consumption while O females showed an increase in oxygen consumption.

Oxygen consumption levels per mouse and per gram during recovery from thiouracil rose and sometimes reached levels existing prior to thiouracil treatment for W and O males and females.

Thiouracil was goitrogenic in all groups of mice, and thyroid size was reduced in all on recovery from thiouracil. Asphyxiation time was reduced on recovery from thiouracil.

The data presented in this thesis can be considered as consistent with the literature with regard to control rates of oxygen consumption, with regard to the goitrogenic action of thiouracil in mice and the difficulty of decreasing the rate of oxygen consumption in mice by the

administration of thiouracil. Oxygen consumption depended upon the relationship between quiet, sleep and activity. Body weight, ambient temperature and the relationship to time of feeding also were factors contributing to variability.

New information developed includes the establishment of strain and sex differences in oxygen consumption rates, asphyxiation times and the action of thiouracil.

While oxygen consumption per gram of mouse per hour was similar for males and females of the W and O strains, the items physiologically integrated into oxygen consumption must have been different as indicated by the differential effects of thiouracil on oxygen consumption (increase in O females; decrease in W females, O males and W males).

There was no significant correlation between asphyxiation times and oxygen consumption rates.

Sex, strain and thiouracil were factors in the differences noted in oxygen consumptions, asphyxiation times, and thyroid weights. Sex was the most potent factor of the three on asphyxiation time differences; strain was the most potent for oxygen consumption differences and thiouracil for thyroid weight differences.

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