A STATISTICAL ANALYSIS OF THE SIZE-DEPENDENCE OF METABOLISM UNDER BASAL AND NON-BASAL CONDITIONS

THESIS

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CHAPTER 1

INTRODUCTION

It is remarkable that the great philosopher Aristotle, who definitely was the first man ever to study the human being and its organization in a logic manner and was so keen in proposing theories, never mentionned anything about breathing and Science had to wait centuries until Lavoisier made the first experiment on respiration. It is true however that other people in the meanwhile have talked about the " Breath of Life " mostly in a mystical way, but their considerations were so devoid of scientific foundations " that they can have now but little value except as an historic record of the trend of scientific thoughts at that time " . (Benedict, F.G. 1935.)

So Lavoisier was the first man ever to consider oxygen as a " burning fuel " of the body. So advanced was he in his theories that, as reported by Seguin, a co-worker, not only did he realized the role of oxygen in the body, but he fabricated a copper mask, held in place about the neck by cement

and attempted direct measurements of oxygen consumption and carbon dioxide production. The study of metabolism of liv ng beings had started.

The study of metabolism and its variations brought the biologists to consider different factors to explain its varying rate in different animals. Rameaux and Sarrus, two french biologists, were the first to consider metabolism in its relation to body size. In fact, in a paper published in 1838 and submitted to the " Académie Royale des Sciences " they deduced mainly from philosophical and mathematical considerations, that metabolism would depend on the surface of the animal and not on its volume (weight). This was the beginning of the so-called surface-law. Later on, Richet, in 1888, published in France a survey of all the work done on this subject up to that time, and Rubner's celebrated experiments on dogs (1894) and other mammals established the surface law as a general principle in the relation between metabolism and body size, especially in homeothermic animals.

From the results of modern research, it appears that there is no general rule for the relation between metabolism and body size. In intraspecific comparison, that is, comparing the metabolism of animals of the same species and of different size over the growth period, different forms of the

size-metabolism relation are found in the different classes of the animal kingdom.

In this way, Bertalanffy (reviews 1949 and 1951.) based upon an extensive material representing many invertebrate as well as vertebrate classes, has stated different " metabolic types " with respect to the relation of metabolism to body size, and has shown that they are related to corresponding " growth types " with respect to growth curves according to his theory on the relation between metabolism and growth:

First type : Respiration following surface rule or 2/3 power of weight. Holds for vertebrates, especially fish, and certain invertebrates such as crustaceans, clams, etc.

Second type: Respiration proportional to weight itself: insect larvae, Orthoptera, Helicidae.

Third type : Respiration intermediate between the two previous types, i.e. $2/3 < q < 1$: Planorbidae, Limnaea. (1)

Interspecific comparison, i.e. comparison of metabolism of mature animals of different species, shows that the relation between basal metabolism and body size in mammals

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1 - Cf. equation (1) p. 19.

follows rather a 3/4 power rule rather than the surface or 2/3 power rule. This was established in interspecific comparisons by Kleiber (1932, 1947.) and independently by Brody (1945) and it correspond also to the extensive work of Benedict and his co-workers (1) (1938) notwithstanding the latter author's scepticism against logarithmic expressions of the relation between metabolism and body size.

Considering intraspecific comparisons of growing mammals, it is surprising how small is the number of available modern data and how little consistent they are notwithstanding the fact that is was mammals which gave the primary basis for stating the surface rule. In a review on the subject, Kleiber (1947, cf. p. 531) mentions that " in the three species, mice, rabbits and dogs, the differences in size are considerable and an analysis of the relation between body size and metabolic rate within these three species seems more promising than in the other species with more uniform size ".

The regression line for metabolic rate of mice given by Benedict (2) (1938) as a function of their body weight would indicate a function: $Weight^{0.89}$, would best fit the

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1 - See Figure 1 page 11.
2 - See Figure 2b page 13.

data. Kleiber is of the opinion however that these results were affected by a group of four endocrinologically abnormal dwarf mice. If the regression line is estimated through the other results, the best fitting power function then would be 0.76.

According to the same author, the regression line given for rats (Figure 2a, p.13) indicates that, intraspecifically, they follow the surface law and their metabolic rate are most nearly proportional to the 0.67 power of body weight.

Regression lines concerning rabbit data were published by Lee (1939) who found that metabolic rate is most nearly proportional to the 0.82 power of body weight although, as quoted by Kleiber, " the range of body size in these rabbits would have to be four times as great as it is, to demonstrate a significant departure of rabbits from the hypothesis that metabolic rate is proportional to the 2/3 power of body weight "

The data on three groups of dogs reported by Galvao (1942) indicate proportionality of metabolic rate to the 0.84 power of body weight, and since the variability in this case seems rather small, the deviation from the surface law and even from the 3/4 power rule appears significant and so does the deviation from the hypothesis that the metabolic

rate of these dogs is proportional to their body weight. These results are not in accordance with the data of Lusk Kunde and Steinhauss as calculated by Benedict (1938) (Figure 1 - shown with other species studied by the same author) who found that the metabolic rate of dogs is most nearly proportional to the 0.55 power of body weight.

So far as small rodents are concerned, there are also the investigations of Carr and Krantz (1945) on ninety two rats and the experiments of Sherwood (1) (1936) results of which appear on Table 1 (p.12) for comparison with Benedict's data as shown in Figure 2, a and b (p.13) (2)

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1 - Sherwood's results were expressed in calories per day and calories per square meter of surface. They were re-calculated uniformly in cc O_2/hr for the purpose of comparison.

2 - All of Benedict's data could not be used in this study because in several instances results were calculated in calories per square meter of surface. Since the evaluation of surface depends on the formula used, results so published cannot be readily compared with other data. This is one of the reason why we have calculated our results in cc Oxygen per hour per total gram weight of the animal.

It is hard to compare Carr and Krantz (1945) results to other data since they are not calculated on a comparable basis (1). However, the mean of the number of calories of heat production they obtained for the twenty four hour period was 1040 calories with a mean respiratory quotient of .725, somewhat higher than Benedict (1938) who had found 880 calories for the rat at 28° C. This difference,however, is due to the fact that different constants were used when calculating the area of the animal (2) since the results are expressed in calories per unit surface. Calculated with similar formulae, the results of Carr and Krantz are very close to the data compiled by Benedict, while Sherwood's (1936)(3) data are slightly lower in values. We find however, that little attention was paid, in all these experiments, to rats below 100 grams in weight, and so small animals did not enter into the final tabulations.

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1 - Carr and Krantz grouped their animals, averaged their weight and averaged their results (for each group) which were calculated either in grams O_2 per 100 gram rat per hour or Calories per square meter per 24 hour. It is only therefore p ossible to compare with mean values for similar groups obtained by other authors. (Results shown in Table 1 p.12 .

2 - The surface area was calculated by the formula set forth by Diak : $S = 7.64 \times W^{2/3}$ for fasted rats.
Benedict used as constant : 9.13

3 - See Table 1, p.12. Re-calculated in cc O_2/hour.

Brody (1945; Kibler and Brody, 1942.) has done extensive work on the subject both on basal and resting metabolism. In his method of calculation (1), he separated the allometric line into several hypothetical sections. While we did not, in this study, find a special exponent for rats of the 20 - 40 gram range, our results for large rats are very similar. In absolute values, Brody's basal metabolism values are somewhat higher than Benedict's (Cf. Figure 2a for Benedict's values and Figure 3 for Brody's) the former however covering a greater part of the weight range of the rat.

Basal metabolism in relation to body size was investigated by I. Mueller and Bertalanffy (2). These data will be used in the course of the present paper.

The present work gives a re-examination of the problem under two viewpoints:

1) The relation of basal metabolism to body size in growing rats and mice is investigated using a sufficient number of animals of varying sizes to determine exactly this relationship.
2) The question of the dependance of the size-metabolism relation under varying conditions is hardly investigated as yet. For this reason, that relation was studied not only under basal conditions, but

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1 - In this study the same method of calculations was used.
2 - Results unpublished.

also under different conditions of temperature nutritive status and exercise.

Total metabolism, in homeothermic animal, can be considered as composed of the following main components:

Total metabolism = Basal metabolism + expense for digestion + expense for thermoregulation + expense for external work.

Basal metabolism measured as Oxygen consumption, calories or CO_2 production, is defined as the minimum metabolic rate under the conditions of fasting, rest and thermoneutral environment. In a mature animal it represents the minimum necessary for the maintenance of the organism, including the energy necessary for the minimum functional activity (of the life important organs, heart, lungs, respiratory musculature, liver, kidneys, etc.) and for the constant renewal of tissues. In a growing organism, the energy needed for the synthesis of building materials and growth is to be added. The amount of energy needed for protein synthesis, with respect to maintenance and growth, appears however, to be small as compared to the other components of metabolism.

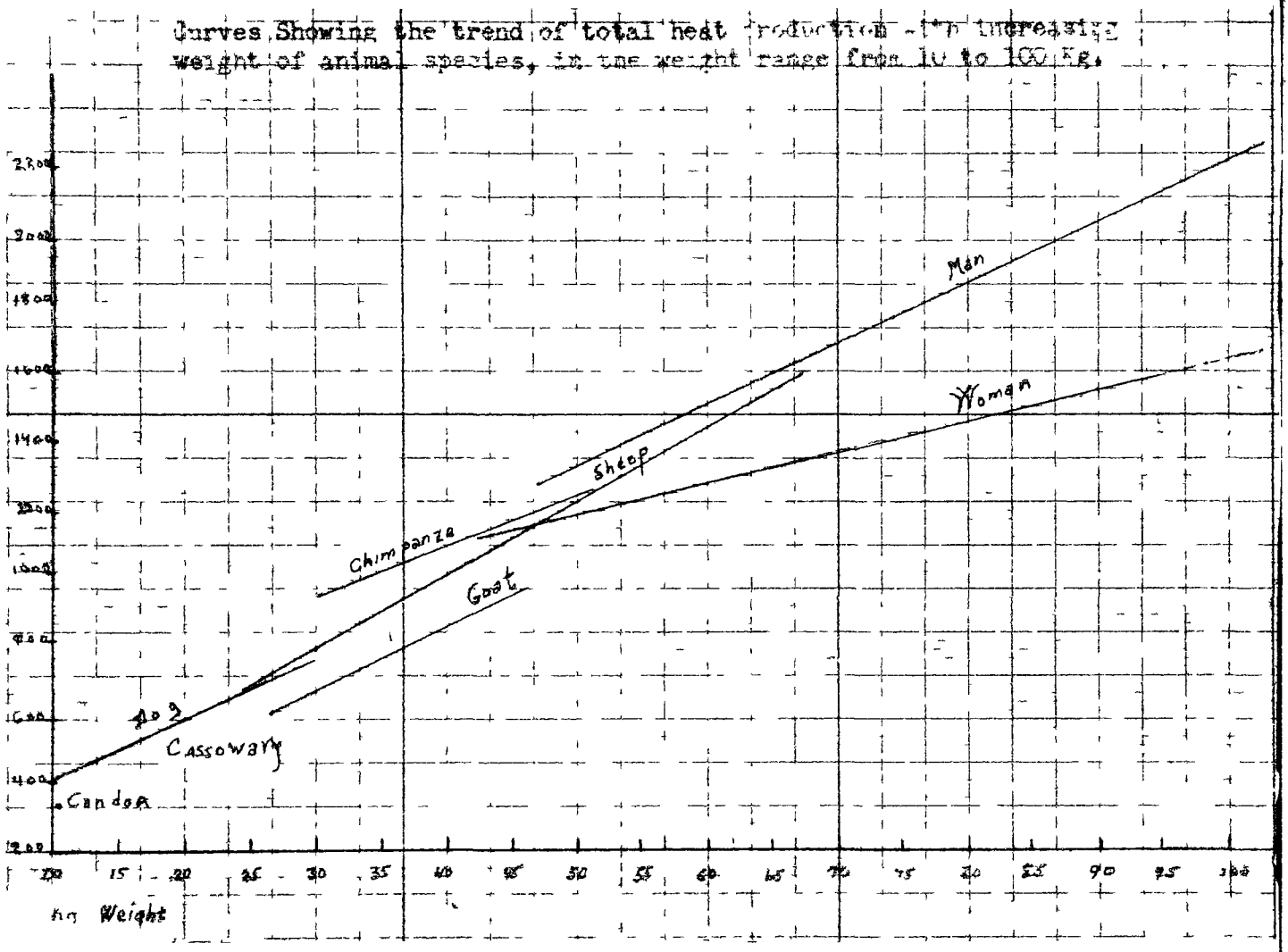
If the animal is not fasting, its metabolism is increased owing to the work of the intestinal tract, gland secretion, etc, and to the specific dynamic action of proteins

(if any). Thus resting metabolism is defined as metabolism under the condition of non-fasting, but inactivity and thermoneutrality.

If the environment is not thermoneutral, additional energy is needed for thermoregulation. Correspondingly, muscular work naturally increases metabolism.

It is one of the main results of the present study that the size-metabolism relation varies for different metabolic conditions.

Figure 1



Reproduced from Vital Energetics, by Benedict F.G.
Carnegie Institute, Washington, 1938.

TABLE 1

Results obtained by Carr and Krantz

Body weight	Gm O_2 per 100 gm body wt per hr.	Average Body Weight
91 - 177	0.143 - 0.268	143
93 - 164	0.120 - 0.221	125
108 - 163	0.155 - 0.233	131
112 - 154	0.129 - 0.206	129
120 - 185	0.189 - 0.266	170
120 - 201	0.150 - 0.211	161 (1)

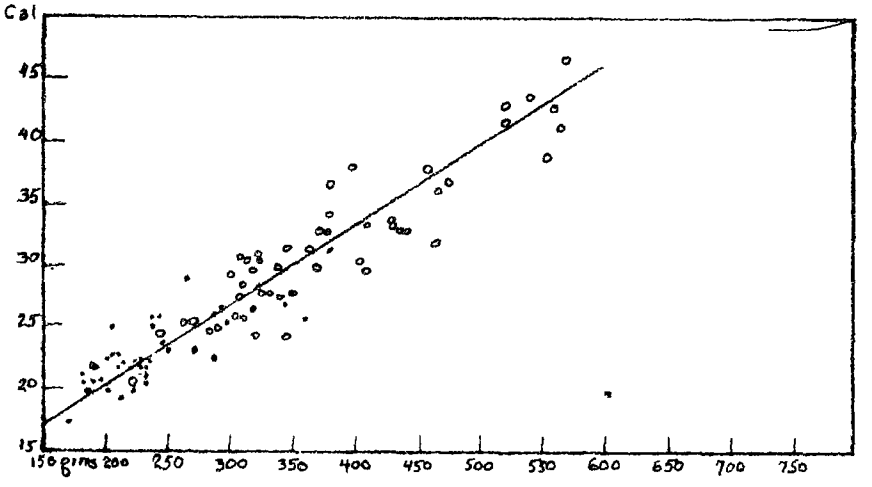
(1) Probably not fasting.

Results obtained by Sherwood

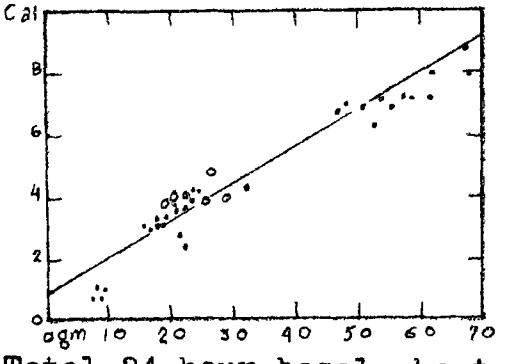
Males			Females	
Cc O_2 pr.hr	Calories per kilo per hour	Weight	Calories per kilo per hour	Cc O_2 pr. hr.
183.2	6.63	131	6.77	187.1
182.8	6.37	136	6.10	175.
190	6.17	146	6.07	187
187	5.87	151	5.70	181.5
174.3	5.23	158	5.38	179.3
187.5	5.29	168	5.39	191.
191.1	5.33	170	5.22	187.2
189.4	5.13	175	5.19	191.6
190.5	5.03	179	5.03	190.5
207.3	5.20	189	5.17	206.1
191.2	4.60	197	4.98	207.
201.7	4.53	211	4.62	214.6
227.4	4.90	220	4.93	228.8
226.	4.74	226	4.64	221.2
244.4	4.69	247	4.48	233.4
251.7	4.52	264	4.01	223.3
270	4.62	277	4.30	251.2
254	4.17	289	4.05	247
264	4.15	302	4.00	255
268.1	4.18	304	3.84	246.3

Figure 2

Results obtained by Benedict (1)



Rats - Total 24-hour basal heat production referred to body weight. Hollow circles represent males, solid dots, females.

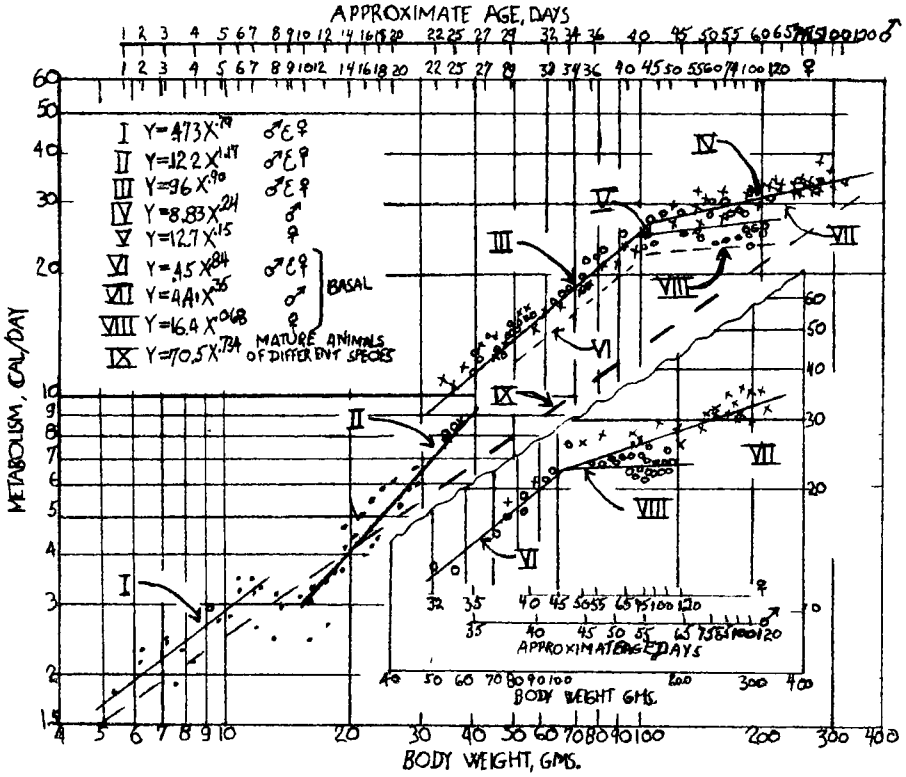


Mice - Total 24-hour basal heat production referred to body weight. Solid dots represent Benedict's data, hollow circles, values of Ebelling and Corey.

~~1 Tabulation of the results are given on page~~

Figure 3 (1)

Results obtained by Brody.



1 - Reproduced from S. Brody, Bioenergetics and Growth 1945. Reinhold Publishing Corporation.

CHAPTER II

METHODS AND MATERIAL

Rats

White rats of the Wistar strain, bred in this laboratory, were used for the experiments. The animals were fed on Purina Chow. The experiments were done at a temperature of 29° - 30° C. which for rats corresponds to thermoneutrality. For basal metabolism determination, the animals weighing more than 60 grams were fasted for 18 hours prior the experiments, while those of less weight were fasted for periods of 6 to 8 hours at the most. For the determinations done in summer, the rats were given a climatization period of 15 - 18 hours at 26° - 28° C. prior the experiments. The animals were left in the respirometer for one to two hours before starting the determinations. Oxygen consumption as well as CO_2 production were measured, giving respiratory quotients varying between .70 to .94 . Experiments giving a respiratory quotient greater than .80 were discarded. Since, as is well known, the metabolism of rats shows a diurnal cycle (Brody, 1945) all the experiments were carried through between 10 A.M. and 4 P.M.

Because, further, " the timing of the rythmic activity in animals, depends on the nature of their visual apparatus " all experiments were carried through in bright light.

For non-basal conditions, all animals were fasted for ten hours and then given food ad libitum and the experiments were done 45 - 60 minutes after feeding. This procedure was applied in order that all animals eat prior the experiments. Of course there is no guarantee that they were all at the same stage of digestion, and this may possibly account for the scattering of the results. (Table IV, p 40, Figure 11 and 12, p. 45 and 46.)

As additional data, a series of determinations (unpublished) carried through by I. Mueller and Bertalanffy at Zoological Institute, University of Vienna, Austria, was used. These experiments were done with a small race of albino rats, inbred for years at the Vienna Zoological Institute. There are obviously genetic as well as environmental differences between the Vienna and the Ottawa experiments. The nutritional status of the Vienna animals was much poorer (1) than that of the Ottawa rats, the first being fed a mixed diet of bread, potatoes, oats, vegetables, meat, twice a week with additions of vitamins. The experi-

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1 - Personal communication.

mental procedure was similar to that applied in the experiments described above. Animals under 40 grams in weight were fasted 5 - 6 hours, larger ones, fasted for 17 - 22 hours. The determinations were made at a temperature of 27° C. (slightly less than in the present experiments) . No attention was given to obtain minimum values, but the values indicated in Table 11 are simply averages of the experimental period of ½ hour (periods of activity excluded) .

Mice

For these experiments, albinc mice, inbred for generations at this Department, were used. They were fed on Purina Chow. As much as possible, different animals were used in all experiments in order to exclude individual differences. However, usually three determinations were made with the same animal to provide sound averages. No special selection was applied besides excluding individuals fighting each other, too quiet, or showing other signs of abnormality . Pregnant females were included in the general graph for females.

In basal metabolism determinations, animals smaller than 10 grams were fasted for 6 hours, those of a larger weight, were fasted for 12 hours. Water was provided ad libitum. Experiments were made at a temperature of 30° - 32° C. In the experiments done during the summer, the animals

were given a climatization period of 15 - 18 hours at 26° - 29° C. p rior to experiment.

In the experiments with exercise, only males were used because of the difficulty of getting large females to run regularly. Small animals usually, needed little training while those of weights between 15 - 25 grams had to be given several exercises before running without interruption or " riding the cage " .

Calculation of the results.

As mentioned above, the usual duration of an experiment was one hour, six determinations being taken at a 10 minute interval, and periods where the animal was not at complete rest, being discarded. For the purpose of the calculation of the regression line, an average was taken of the three determinations (each of 10 minutes) lying closest to each other and from this average, O_2 consumption per hour was calculated. Naturally the average so calculated does not give the lowest absolute values observed, but it was deemed that this way of calculation gives the most consistent values considering the variations during one, and of the different experiments.

The dependence of metabolism on body size is best determined by an allometric plot. Metabolism being proportio-

nal to some power of weight, we have:

$$Y = b X^a \qquad (1)$$

where Y is the metabolism of the animal, X the weight, b and a constants. According to:

$$\text{Log } Y = \log b + a \log X \qquad (2)$$

the logarithmic plot gives a straight line, the slope of which yields the relation wanted. A tangent $a = 2/3$ indicates proportionality to surface while tangent $a = 1$ indicates proportionality to weight.

Since the equation (2) has two unknowns, we must have two equations to solve it. These two normal equations are obtained by multiplying the equation first by the coefficient of log b (which is unity) and then by the coefficient of a (which is log X) . We thus have:

$$\text{Log } Y = \log b + a \log X$$

ans summing up all the points:

$$\Sigma \text{Log } Y = N \log b + a \Sigma \log X \qquad (3)$$

where N is the number of points in the graph. This is our first normal equation. Multiplying (2) by the coefficient of a to get the second normal equation we have: (after summing up for all the points)

$$\Sigma \log X \log Y = \log b \Sigma \log X + a \Sigma (\log^2 X) \qquad (4)$$

Dividing equation (3) by N and equation (4) by $\Sigma \log X$ and then subtracting (3) from (4) we eliminate unknown

log b and then can solve for a . We solve for log b by replacing proper value for a in any one equation. Equation (1) is then solved, Y and X being measured, b and a calculated as above.

We now need a test to ascertain the scatter of the data points about the regression line expressed by the equation (1). This test is called the Standard error of estimate the formula for which is:

$$S^2_{yx} = \frac{d^2}{N'} \qquad (5)$$

in which d represents a single deviation of the actual value of Y from the value computed from the equation, N' is the " degree of freedom " (which is expressed by the number of data points less the number of constants in the equation) . The following general formula is used to solve the problem:

$$S^2_{\log y \log x} = \frac{\sum(\log^2 Y) - \log b \sum(\log Y) - a\sum(\log x \log y)}{N'} \qquad (6)$$

The standard error, thus calculated, is the difference between two logarithms, since the difference between two logarithms is a ratio, to express the standard error in percent we must assume a base such as 100 along the equation line to work from. The logarithm of 100 is 2.0000, adding the standard error obtained from the above formula (which is e.g., .055 for male rats in summer) we have 2.055 . The antilog of 2.055 is 113.5 or a positive error of 13.5% . Similarly, the negative error is calculated by subtracting 0.055 from 2.0000

giving a negative error of 11.9%. The value of the standard error of estimate means that two thirds of the time the metabolism computed from this equation will agree with the observed metabolism within + 13.5 % and - 11.9 % .

The coefficient of correlation, expressed by ρ can be calculated with the following formula:

$$\rho^2 = \frac{a\ (\sum \log x \log y)}{\sum \log^2 y} \qquad (7)$$

which are values already used in the course of solving equation (1) and the standard error of estimate (6) (p. 19 and 20.) This mathematical treatment follows the procedure as indicated by Bordy (1945, pp. 398 ff) .

Basal metabolism values, measured in cubic centimeter of O_2 per hour can be transformed into calories on the basis of 4.7 calories per liter of Oxygen at a respiratory quotient of approximately .70 . Calories per day should not be calculated from the experiments lasting one hour, since such values would not represent a true metabolic picture for a whole day because of the diurnal cycle in metabolism of rodents.

Preference was given to the expression of values in terms of weight instead of terms of surface, the weight of an animal being a better criterion of comparison that the surface. Futhermore, different authors apply different formulae to calculate surface and such calculation appears to be problematic

in view of the differences of true surface and radiationg surface and various types of insulation like furs, tissues, etc.

All values before plotting were reduced to Normal-Temperature-Pressure (0° C. and 1 atmosphere) and the table of Bordy (1945, p. 320 f.) was used for this purpose.

CHAPTER 111

THE APPARATUS USED (1)

This chapter contains all the pertinent data, i.e. description, capacity, functioning procedure of the apparatuses used. For the sake of clarity, it has been divided into three sections:

1) A general description of the apparatus used.

11) Explanations on the functioning.

111) Capacity of the apparatus used.

Since all the experiments were carried out with the types of apparatuses illustrated in Figure 4 and 5 along with a few improvements as we became acquainted with the problems involved, description will be given in the first section of only one apparatus used, mentioning the features which caracterize the others.

The second Section will deal with general notes and comments on the functioning and special arrangements of the apparatuses, while the third Section will show the theoretical capacity of the apparatus in the light of pump/animal container ratio.

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1 - A description of a similar apparatus has been given by Benedict (1930).

Section 1

A general description of the apparatus used.

Since in our experiments it was necessary to obtain accurate measurements of the oxygen consumed at different temperatures and the amount of carbon dioxide produced in order to calculate the respiratory quotient, it was decided to use the closed system apparatus.

In this system we have a pump which circulates the internal atmosphere of the animal container through a carbon dioxide absorbing solution and returns it to the container. As CO_2 is absorbed the internal pressure decreases and oxygen is released from a reservoir to the animal chamber or heating chamber, so that the internal pressure is kept within fixed limits with respect to the atmospheric pressure. In this way, O_2 consumption is measured in cc of a water column; CO_2 production is measured by titration of the barium hydroxide used for absorption.

Thus we see that the apparatus is composed of three different parts:

a) The animal container and its accessories.

b) The purifying system.

c) The oxygen supply system.

Each of these parts are closely interlocked and calibrated

in such a way to suit the animals under experimentation and obtain sound results.

a) The animal container and its accessories.

The animal chamber was a glass jar of about two litres in capacity and large opening. In order that the animal does not rest on the glass, (1) a small screening covered the bottom of the jar or better yet the internal bottom part of the jar was heavily aluminum coated. The top was a heavy rubber stopper and gave an air tight fit with the jar at the same time carrying the accessories and the tube openings to the chamber. The thermometer, calibrated to $\frac{1}{4}^{o}$ C. was pushed in the animal chamber through the rubber top about three inches while the internal part was covered with a small wire mesh to avoid direct contact with the animal in the chamber. The manometer was also connected through the rubber top (See figure 4). It is important that the manometer be as close as possible to the animal chamber and that the connecting rubber tube be quite large and not curved to show exact pressure variations in the chamber in little delays.

b) The purifying system.

The purifying system which communicates through the rubber stopper to the animal chamber comprises: the pump, the

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1 - A rat or mice is always scared and tensed when walking on a smooth surface like glass. Screening makes them comfortable.

carbon dioxide absorbing tower, the moisture absorbent and the heating chamber.

The pump was a Rotaerator, modified, diaphragm type, air proof, 1,600 cc capacity per minute. Since the motor was mounted on a different base from the pump itself, the circulating air was practically unheated at the outlet which was an important factor in the low temperature experiments.

The carbon dioxide absorbing tower contained the hydroxide through which the air was circulated and CO_2 absorbed. Several hydroxides were tried (KOH, NaOH) before selecting barium hydroxide for its sensitivity. To increase the surface absorption of the liquid, about 50 cc of glass beats were inserted in the tower with the liquid.

The water absorbing tower contained approximately five grams of calcium chloride (porous) placed between two pieces of cotton to avoid circulation of chloride dust to the animal chamber (which provoques irritation to the animal).

The heating chamber, used only on the apparatus for rats (Figure 6) was made as small as possible. For this purpose, an ordinary glass jar 100 cc was used with a 30 watt carbon light, placed inside. Since much of the heat produced by a lamp is, by conduction, absorbed by the socket, the connecting wires were soldered directly on the lamp base and no socket was used. The heat thus produced could be absorbed only by the

circulating air and the container. A switch was placed in the lamp circuit and could be thrown in the"off" position when the proper temperature was reached.

An important factor is the size of the tubing between each one of these parts. Since it is desired to have the animal at complete rest, under basal conditions, we can hardly tolerate the animal being in a constant draught. This is particularly important in the case of mice who are very sensitive to air movements. In order to lower the speed of air at the animal container, very large tubing must be used. In the case of the apparatus shown in Figure 5, which was used for mice, this has been achieved by placing the carbon dioxide absorbent in the same container as the animal. Since the inlet of the pump is connected to the top of the bell (glass container) and the outlet at the bottom, (inside the carbon dioxide absorbent) the entire animal chamber can be considered as the return tube for purified air, (1) since the bell has a cross area about two hundred times larger than the tubing used, the speed of air around the animal is considerably decreased. This is the main difference between the purifying system of the apparatus used for rats and the one used for mice.

c) The oxygen supply system.

This supply system is formed by an ordinary 250 cc or

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1 - In this case there is no return tube for purified air since the CO_2 absorbent is placed inside the animal chamber.(Fig.5)

500 cc bottle which has been previously filled with pure oxygen. The top of the bottle is connected to a water burette (filled with ordinary water). As water goes in the bottle, by displacement, when valve D in Figure 4 is opened, oxygen will enter the heating chamber (shown in Figure 6) if this is incorporated in the apparatus or the animal chamber (Figure 5) in the case of mice. A manometer can be attached if desired to the oxygen container to indicate the pressure conditions of the oxygen - it should be filled with Brody's solution and not mercury since the variations are very small. It is also important that the oxygen pressure - before letting in water - be equal to atmospheric pressure. If not, we would not know the true amount of oxygen going to the animal.

Section 11

Explanations on the functioning.

The apparatus was designed so that an animal could be placed in the chamber without having an experiment under way. In fact, by closing valves C, A, F, and opening B, D, E, in Figure 4, the barium hydroxide tower is by-passed and the circulation of air is established with the atmosphere. This permits to choose the conditions we want the animal for investigation, wether complete rest, awake, quiet, etc. This also permits to give the animal a certain time to climatize itself to the chamber before starting an experiment, an important factor since

rats and mice never rest well when they are transferred from one place to another. This temporary excitement disappears, however, after the animal is climatized to it's new place.

Because oxygen readings can be taken at any desired interval, e.g., every five or ten minutes, it is possible to plot oxygen consumption curves for single experiments, while for carbon dioxide values, the entire experiment has to be completed before titration is done. This is a reason why it is important to provide the apparatus with special means for by-passing the carbon dioxide absorbent as the animal's state varies during the experiment and periods when the animal is not at rest are to be excluded. Otherwise the results of titration would be mere average values under varying conditions, while what we desire is true values for determined conditions.

Section 111

Capacity of the apparatus used.

As mentioned in Section 1 of this Chapter, we used in this study the closed system apparatus. In this system, since we are returning to the animal chamber the internal atmosphere after purification, we shall be facing the dilution principle, i.e. the pump will only circulate in a given time a percentage of the air present in the entire system and the hydroxide will only absorb a percentage of the CO_2 present in the circulated air. Making the absorption of CO_2 as perfect as possible we see that

the two controlling factors will be the capacity of the pump and the size of the animal container. The quantity of carbon dioxide removed at any time can be calculated as follows;

$$\left[\frac{\left(\frac{a+b-c}{60}\right)}{P}\right] K_t\ CO_2 = \text{cc of total } CO_2/\text{ sec.} \quad (8)$$

where a = the capacity of the animal container; b, the capacity of all connected vessels in the purifying system; c, the space occupied in all these containers (animals, chemicals etc); P, pump capacity in cc per second and K_t the concentration of CO_2 at any t time. Factors a, b, c, are divided by 60 to express them in cc/second (same basis as the pump). $K_t\ CO_2$ (when there is an animal in the chamber) is the animal production of CO_2 per unit time (expressed as a concentration).

When there is an animal in the chamber, there is accumulation of CO_2 at the beginning of the experiment. Because of this increased concentration, the percentage of CO_2 removed is increased. This state of increasing concentration will continue until the CO_2 produced by the animal equals the CO_2 removed by the hydroxide (1). Then there is equilibrium. The problem thus consist of finding when the system becomes stationary and, what is the concentration, at that time, since it is important that carbon dioxide is not accumulated beyond a certain limit which would cause unphysiological conditions.

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1 - This depends on the capacity of the pump if the chemical has a sufficient strenght.

This brings us to consider if the apparatus has a sufficient capacity to avoid, with a large animal inside the chamber, all accumulation of CO_2 beyond 2 %. Figure 7 shows curves of animals rejecting (a) 300 cc/hour (1) and (b) 150 cc/hour. It can be seen that in the case of (a), when the system stabilizes itself, the concentration is only 0.33 % which is much below our limit of 2 % CO_2 concentration.

To be sure that carbon-dioxide absorption is maintained at a high level, a small amount of barium hydroxide can be placed in a small tube (2) on the path of the outgoing airflow. If the carbon dioxide absorption decreases, there will be a precipitate of barium carbonate which will appear in the tube indicating the main solution of the hydroxide is weakening.

The Threadmill

Early experiments of O_2 consumption on running animals, were done with a threadmill (3) immersed in water. The animal chamber consisted of a screened drum revolving inside

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1 - An animal of approximately 275 grams body weight will reject this amount of CO_2 under non-basal conditions (fed).

2 - The barium hydroxide is dissolved in distilled water and filtered. The solution must be changed often if we desire to have good reliability.

3 - This apparatus was borrowed from National Research Council. A full description of it is given by J.S. Hart, (1950.)

a waterproof container. The desired rate of exercise was obtained from a variable speed motor mounted on the screened drum shaft. The internal atmospheric temperature depended on the temperature of the water bath. The purifying system -pump, tube connections, moisture absorbent, etc - and the CO_2 absorbent were essentially the same as described for the other apparatuses. A simpler apparatus (1) was built later on to extend the study to a larger number of animals under a constant temperature.

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1 - Similar to the above description but omitting the water bath and the water proof drum container.

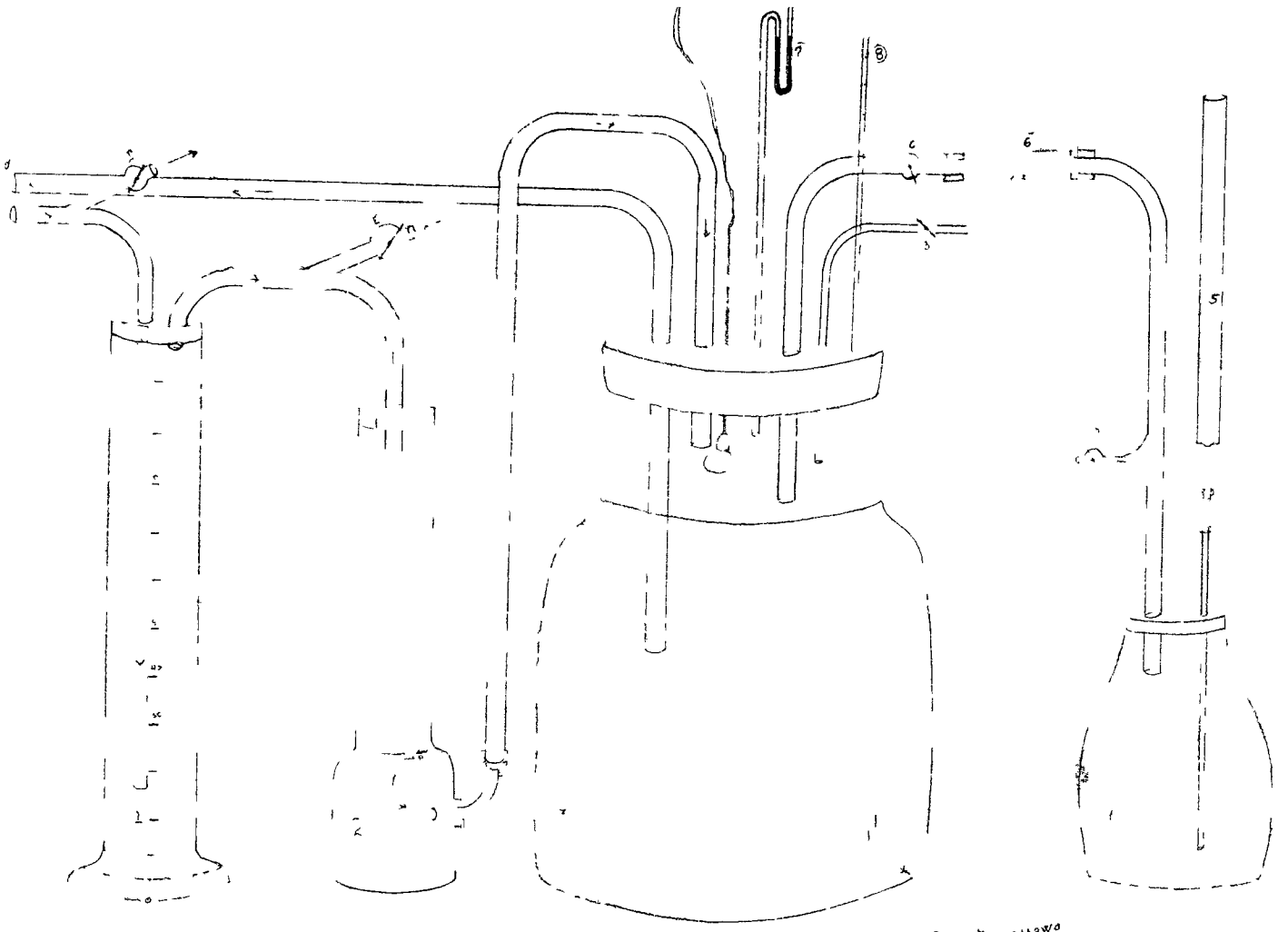


Figure 4 Page 33

Legend

A- Oxygen Refill valve
B- Atmospheric pressure equalizer
C- Oxygen Inlet
D & E- By-pass valves.
F- Water Inlet

1- CO_2 Absorbent
2- Water Absorbent
3- Animal cage
4- Oxygen bottle
5- Water burette
6- Oxygen dryer
7- Manometer
8- Thermometer

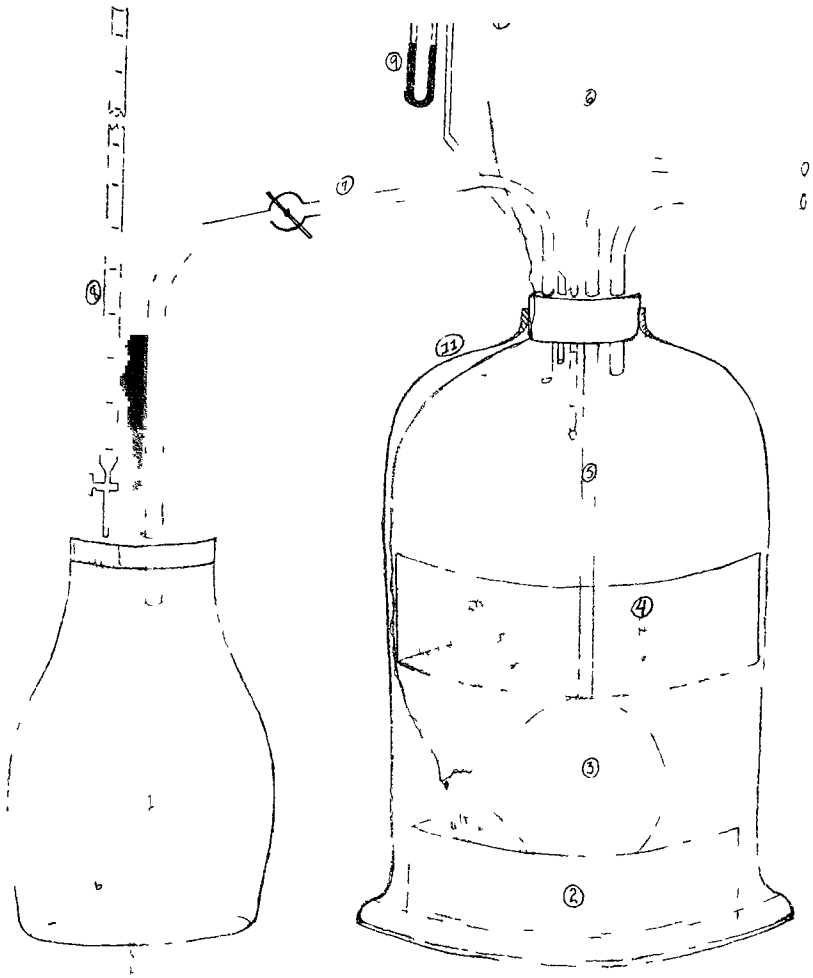


Figure 5

G. Racine
University of Ottawa

Legend

1- Oxygen bottle
2 CO_2 Absorbent.
3 - 20 25 watt bulb
4 - Animal Screening
5 Air inlet - from pump to CO_2 Absorbent
6 Thermometer
7 - Oxygen inlet Line with valve
8 Water burette.
9 Manometer
10 Plug & Line for Lamp inside
11 Glass bell (heavy)

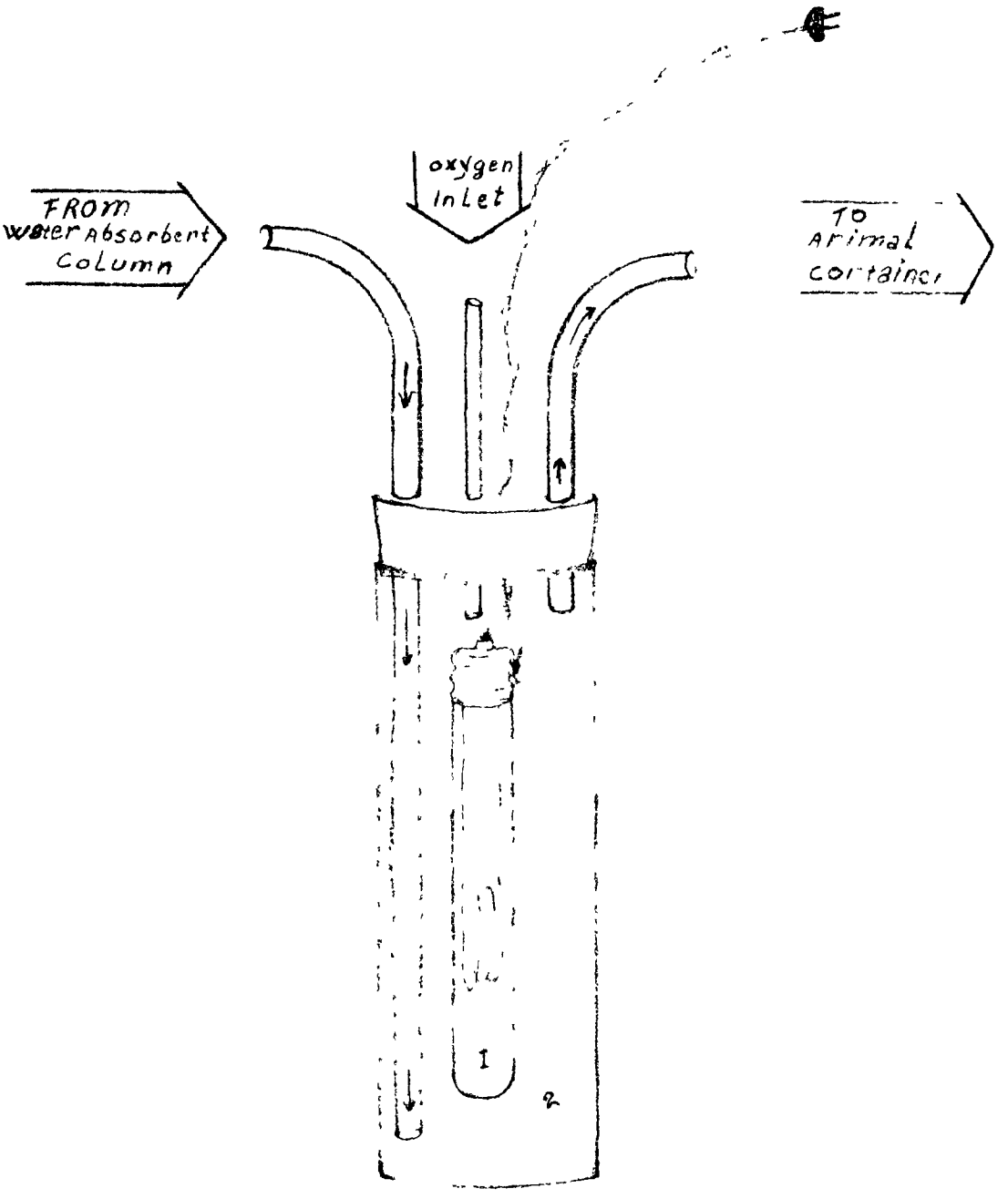


FIGURE 6

Legend

1- Carbon Light used for heating

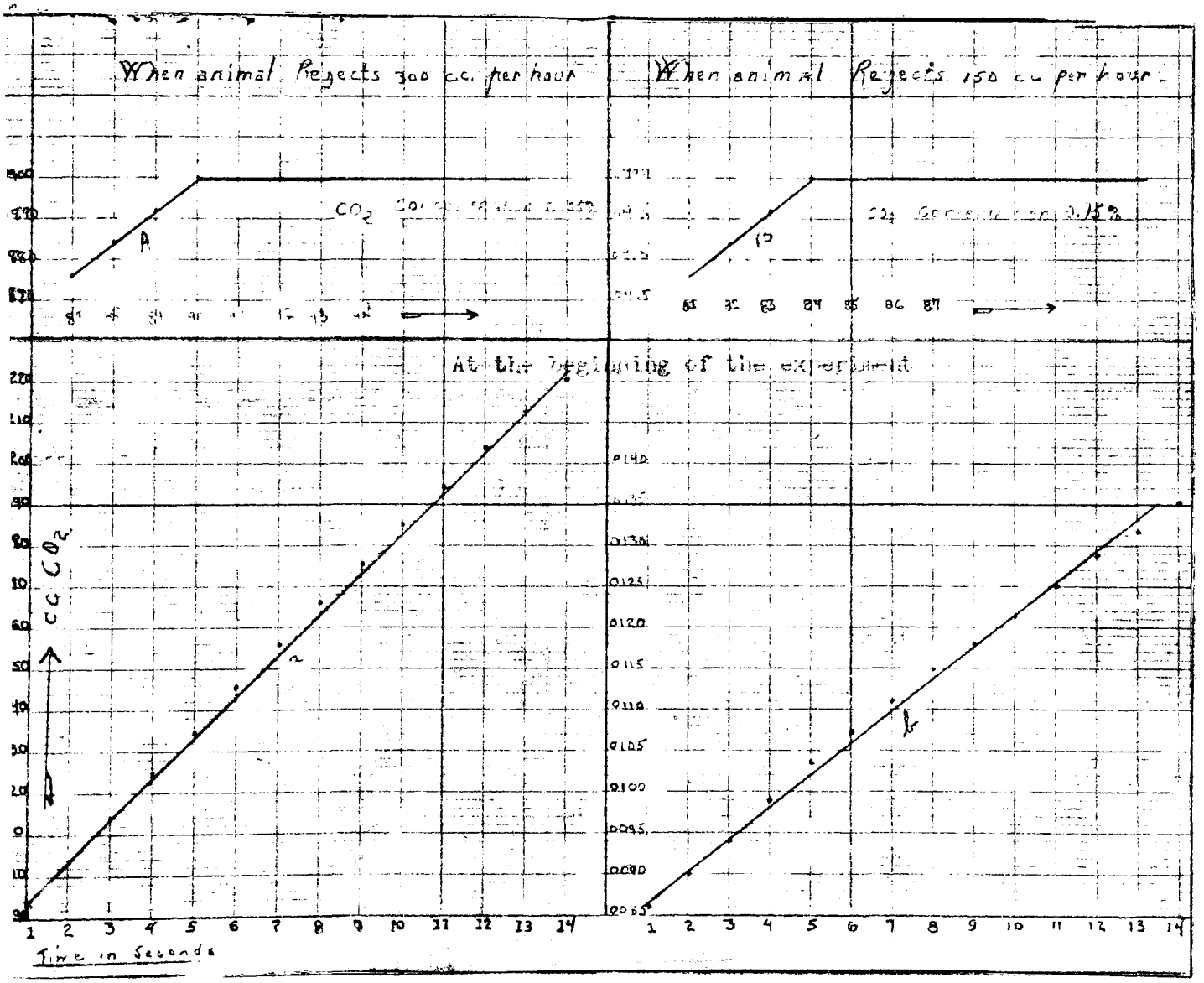
2- Space where purified air is mixed with oxygen

Figure 7

REMOVAL OF CARBON DIOXIDE
FROM ANIMAL CHAMBER

Note: Curve A is the end of curve a . It is interrupted in the middle to show both ends of it:

a) The building up of CO concentration at the beginning of the experiment.
A) The approach to a steady state, after which time the concentration will remain constant, the pump removing the same quantity of CO_2 that the animal is producing.



CHAPTER IV

RESULTS

Rats, Basal Metabolism.

The average O_2 consumption for 1 hour, calculated according to procedure outlined on page 17, is given in Tables II and III, (pp.43-44) with the average respiratory quotients of the animals considered. The statistical evaluation, indicating values for α (slope of the regression line), b (integration constant), $S_{\log y \log x}$ (Standard error of estimate) and ρ (correlation coefficient) can be found in Tables V and VI (pp.52 - 53) while the results are plotted in log-log scale in Figures 8 - 14 (pp.46-49). From this material, the following facts can be seen:

1) Comparing the summer and the winter series of experiments it appears that O_2 consumption in winter is slightly higher than in summer, especially in so far as small animals (1) are concerned. As previously mentioned (page 15) the animals were given, in the summer experiments, a climatization period at 27° C. prior the experiments. It cannot be said from the present experiments wether the effect mentioned is due to the

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1 - Up to 100 grams.

seasonal variation, to climatization, or both; but it can be seen that keeping at higher temperature lowers slightly metabolism especially in small animals where consistent differences of the order of 10 to 17% were found as compared with Sherwood (1936) who found differences of 26% when measured in calories per unit of surface area and 42% when measured in calories per kgr. (1) 2) All series - males and females, summer and winter experiments - show consistently that the slope of the allometric line is steeper in small, as compared to larger animals. For calculation purposes, it was assumed that there is a break in the allometric line at about 110 grams body weight. This, of course, is only a convenient method of presentation, for there is naturally no abrupt change from the first to the second period, nor can it be upheld that the transition occurs exactly at this body weight and corresponding developmental stage. Although fictitious in the sense mentioned, the calculation of two regression lines up to and from 110 grams body weight, clearly shows the character of the relation between metabolism and body size. Up to 110 grams in weight, basal metabolism is approximately proportional to weight ($\alpha \approx 1$) while the slope in the second period, from 110 grams in weight up to the largest animals is much smaller and of the order of $\alpha \approx 0.3 - 0.4$. If however a regression line is calculated for all sizes (which gives of course, a poor fit, being too high for the small and too low for the large animals) its slope is near

1 - The percentage 10 - 17% is calculated from differences of O_2 consumption in cc/hr. Sherwood did not use small animals below 100 grams.

2/3 according to the surface rule (α = 0.57 to 0.71 for the four series of experiments.)

3) Basal metabolism values are not markedly different with respect to the sexes. We do not consider the differences in the individual α and b values with respect to males and females, summer and winter as significant enough to draw further conclusions, apart from the significant differences between the first and second periods as described in 2.

The values of ρ (correlation coefficient) for females over 110 grams are somewhat lower than those for males. This larger scattering of the data for females may be due to the fact that some of the females were in oestrus and thus have a higher metabolism. (1)

Comparing our results with those of former investigations, the following can be stated with respect to the absolute values of our determinations: They are in the range of the basal metabolism values as found by others in rats, although owing to the method of calculation used (see page 18) lower values than ours can be observed and were also found in our experiments. Table XII (p. 61) gives a survey of the different results obtained by several authors using varying methods, while Tables IX, X and XI (pp. 58 - 60) show the range of O_2 variations in the experiments of this study and Table VIII (p. 57) gives the values as calculated from the re gression lines.

There are few data in the literature which give the dependence of metabolism on body size over the entire range of weights. For rats under basal metabolic regime, Kibler and

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1 - Personal communication from Dr. A. Gagnon.

Brody (1945) calculated a slope of the regression line of 0.84 for small animals and 0.35 for larger ones (See Figure 3, p.14) This corresponds well with the present results for animals under basal conditions without climatization period (Winter experiments), 0.93 for small and 0.33 for larger females; 0.94 and 0.32 for males respectively (Table VI, Figure 8 and 9, pp.). The break in the log-log plot at 110 gram body weight is apparent in Brody's as well as in our data. The overall regression in these experiments is 0.56 for females, 0.61 for males; 0.65 and 0.71 respectively for the experiments with climatization (Table V, p. 52) Similarly, Benedict obtained 0.67 this value being computed from two groups of animals.

If we now consider the experiments done by MÜller and Bertalanffy at University of Vienna (1) described on page 16 the computation of which appear in Figure 16 (p.62) we have to notice that these animals are genetically and nutritionally different. The absolute values are higher, owing to the different standards of calculation, as mentioned p. 17. The slope of the allometric line is much smaller (solution gives 0.66 for females and 0.68 for males) in the Vienna experiments, this being explicable as being the gross solution for all animals from 12 grams to 200 grams in weight. The periodization can also be found (Figure 16) the allometric curve becoming flatter with animals 100 - 150 grams in weight, although this could not

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1 - Unpublished.

be calculated since there are no animals of greater weight than 200 grams. These results can be compared with the " slow growth " rats of Horst et al (1934) as illustrated in Table XIII (p.63) Also in Horst's experiments the small slope of the regression line is apparent which gives approximately an $a \approx 0.55$.

Rats, Non Basal conditions.

Under non-basal conditions, that is, animals resting and in thermoneutral environment, but fed, the slope of the regression line is much smaller than under basal conditions. The results of the determinations in non-basal conditions are given in Table IV (p.45). For males under basal conditions, the slope varied from 1.05 to 0.94 for small animals and 0.36 tc 0.32 for larger animals depending upon the climatization the animals received prior the experiments and the season. Under non-basal conditions, this slope becomes 0.5 (Table VII, p.54) for small animals and 0.3 for larger ones (Figures 12 and 13, pp.50 - 51). As can be seen, the slope of the regression line is changed in the small animals, while there is no significant change in the large ones, although, of course, the absolute values are higher under non-basal than under basal conditions.

It seems to be dubious, however, wether the method of calculation, i.e., presupposing two regression lines, one for the smaller and one for the larger animals, is statistically legitimate in the case of non-basal conditions. As seen in Table VII

(p. 54) the ρ values are much lower than in basal metabolism condition (Table V and VI, p. 52 - 53). This is natural since under non-basal conditions a greater variation and less correlation with body weight is to be expected due to the fact that the physiological conditions cannot be completely controlled. However, the ρ values for animals over 110 grams are exceedingly low and the best correlation (highest ρ values) are obtained in the overall regression covering the entire series from 40 - 300 grams. This indicates that the break in the curve at 110 gram body weight, which is marked under basal conditions is rather insignificant statistically under non-basal conditions, while at the same time the size metabolism regression is less than would correspond to the surface rule ($\alpha \approx 0.45$).

Kibler and Brody have studied resting metabolism in which food was given ad libitum . They have obtained (Figure 3, p. 14) slopes of 0.90 for small animals and 0.24 for larger ones. This discrepancy with our results may be due to the fact that Brody's values are for " resting metabolism " and apparently no special care was taken that the animals are in post-absortive condition after feeding, while our experiments were arranged in such a way (page 16) as to guarantee as far as possible that the determinations are taken a short time after the intake of food. (1)

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1 - Brody's values for resting metabolism are shown in Figure 3. (page 14).

TABLE 11

RESULTS - FEMALES

Basal Metabolism

Summer			Winter		
Body Weight in grams	Average used in the computation	R/Q	Body Weight in grams	Average used in the computation	R/Q
28	55 cc O_2	.71	30	64 cc O_2	.70
30	57	.71	37	72	.72
32	62	.74	39	77	.72
35	60	.73	43	79	.70
39.5	67	.76	44.5	80	.72
45	70	.75	46.5	85	.70
48	77	.73	53	92	.71
55	79	.70	56.5	102	.74
57	89	.78	62	115	.75
60	94	.75	71	112	.71
69.5	101	.75	74	126	.75
76	111	.73	80	141	.77
80	124	.75	91	154	.72
90	129	.71	96	170	.75
95	150	.76	105	170	.73
99	175	.76	110	189	.73
105	164	.71			
113	186	.74	120	187	.70
120	174	.72	126	210	.76
126	210	.77	134	188	.73
130	180	.72	151	225	.74
145	220	.72	161	196	.72
150	194	.70	179	210	.74
170	190	.71	185	232	.75
176	220	.75	200	232	.76
190	200	.72	205	210	.71
200	230	.73	246	227	.71
220	197	.70	250	250	.73
250	234	.72	275	260	.71
298	260	.73	297	270	.71
330	275	.74			
348	292	.75			

Averages used for the computation of the regression lines. Respiratory quotient are averages of the three experiments considered.

TABLE 111

RESULTS - MALES

Basal Metabolism

SUMMER			WINTER		
Body Weight in grams	Average used in the computation	R/Q	Body weight in grams	Average used in the computation	R/Q
36	65 cc O_2	.74	37	80cc O_2	.71
38	62	.71	38	80	.71
40	68	.71	39	77	.70
44	66	.72	41	84	.72
45	70	.71	47	90	.72
48	74	.73	50	92	.75
50	78.5	.74	54	97	.77
56	78	.71	59	100	.76
62	90	.75	64	111	.74
68	101	.73	70	121	.76
70	111	.74	74	136	.72
75	115	.72	80	145	.74
81	129	.75	91	150	.72
93	136	.71	100	169	.73
100	158	.74	105	186	.77
105	160	.73			
110	180	.77			
120	170	.72	111	192	.73
131	194	.73	121	196	.73
149	200	.75	136	203	.75
170	206	.71	150	212	.74
190	199	.71	161	215	.76
250	236	.72	180	215	.71
300	262	.71	200	225	.72
			238	236	.74
			251	248	.73
			262	262	.71

Averages used for the computation of the regression lines. Respiratory quotients are averages of the three experiments considered.

TABLE IV

RESULTS - MALES and FEMALES

Non basal conditions

MALES			FEMALES		
Body weight in grams	Average used in the computation	R/Q	Body weight in grams	Average used in the computation	R/Q
43	134 cc O_2	.95	45	121 cc O_2	.91
50	136	.90	50	141	.93
55	170	.96	55	119	.86
60	146	.93	60	159	.94
64	125	.88	66	140	.90
71	205	.98	70	184	.95
77	165	.88	76	141	.84
90	246	.97	89	154	.87
96	171	.90	101	184	.90
100	200	.93	106	225	.90
117	179	.88	125	204	.94
126	295	.98	140	229	.95
131	226	.93	151	200	.90
151	297	.95	181	284	.92
200	317	.91	239	239	.91
171	210	.92	200	249	.89
231	258	.88	280	206	.84
250	350	.90	285	264	.89
281	255	.90	301	369	.86

Averages used for the computation of the regression lines Respiratory quotient are averages of the three experiments considered.

Female Rats

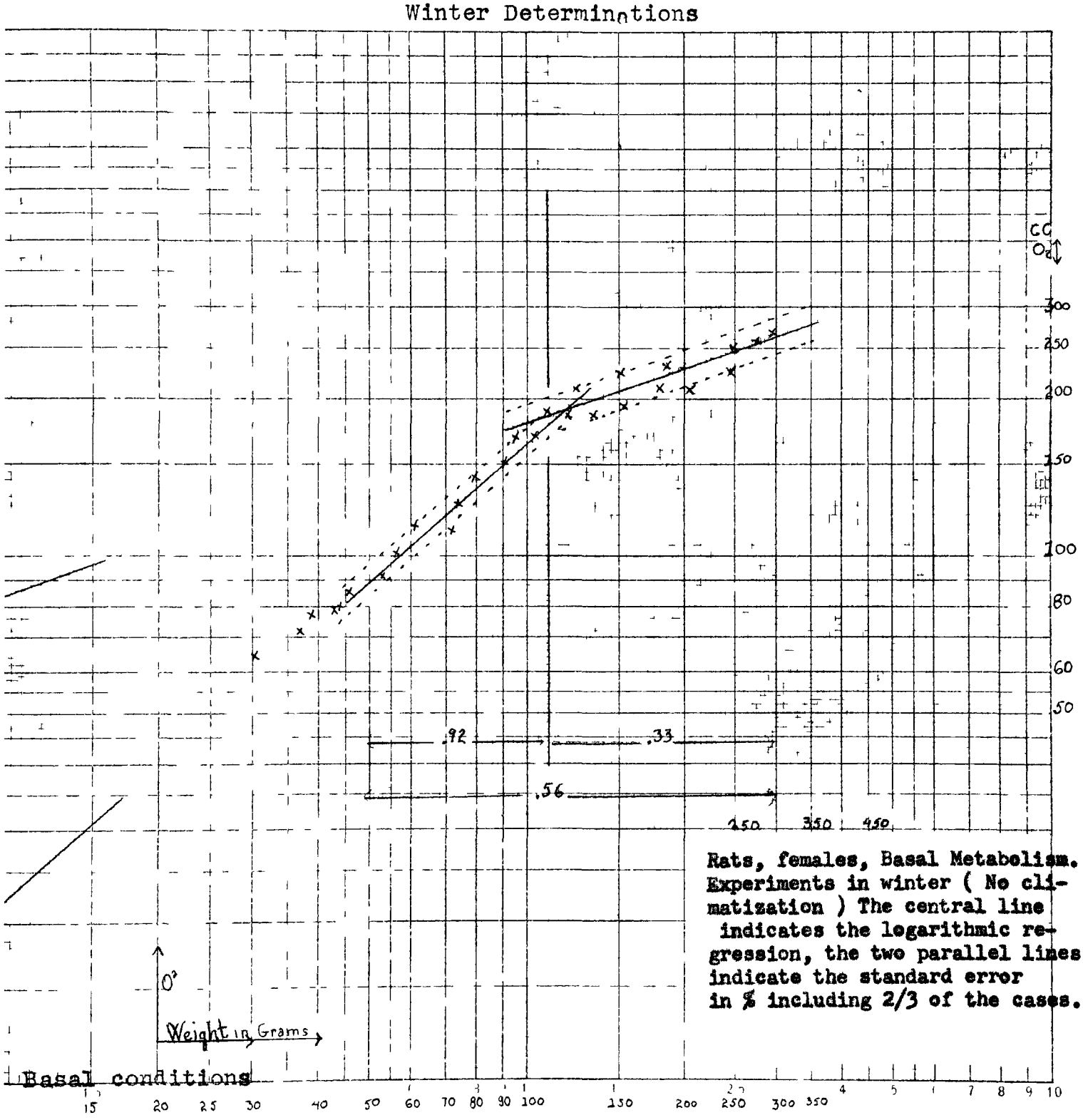
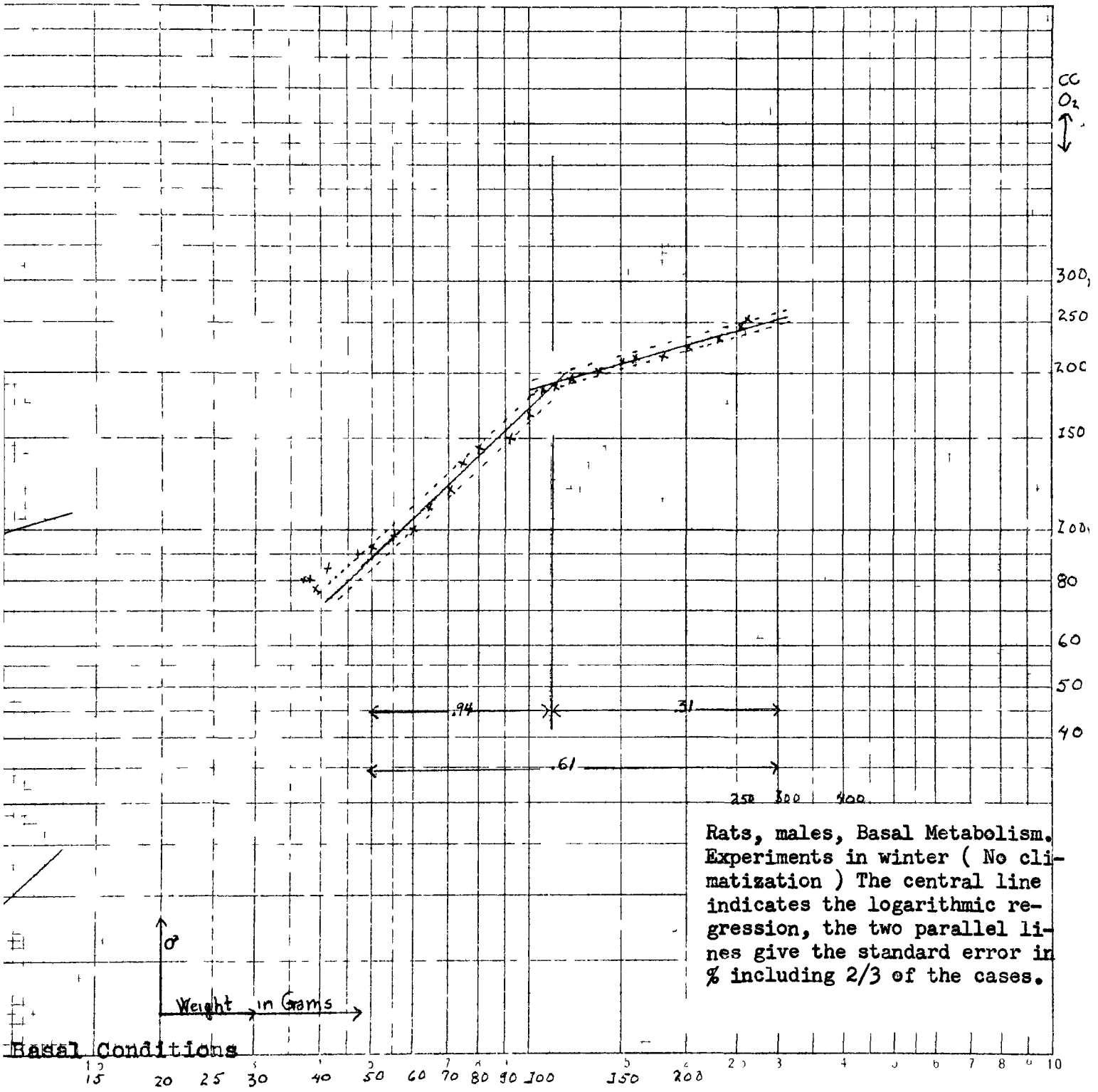


Figure 8

Male Rats

Winter Determinations

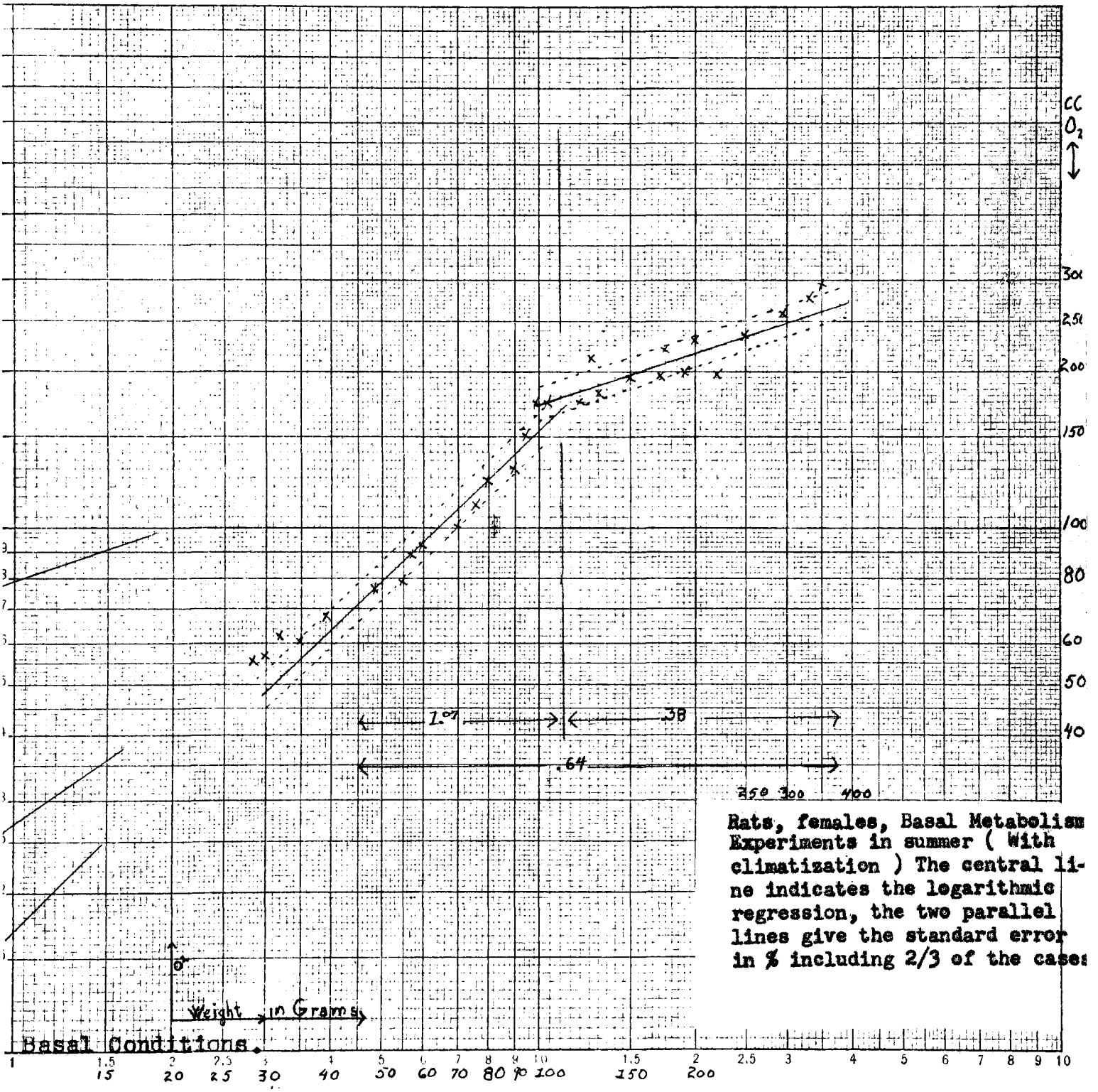


Rats, males, Basal Metabolism. Experiments in winter (No climatization) The central line indicates the logarithmic regression, the two parallel lines give the standard error in % including 2/3 of the cases.

Figure 9

Female Rats

Summer Determinations

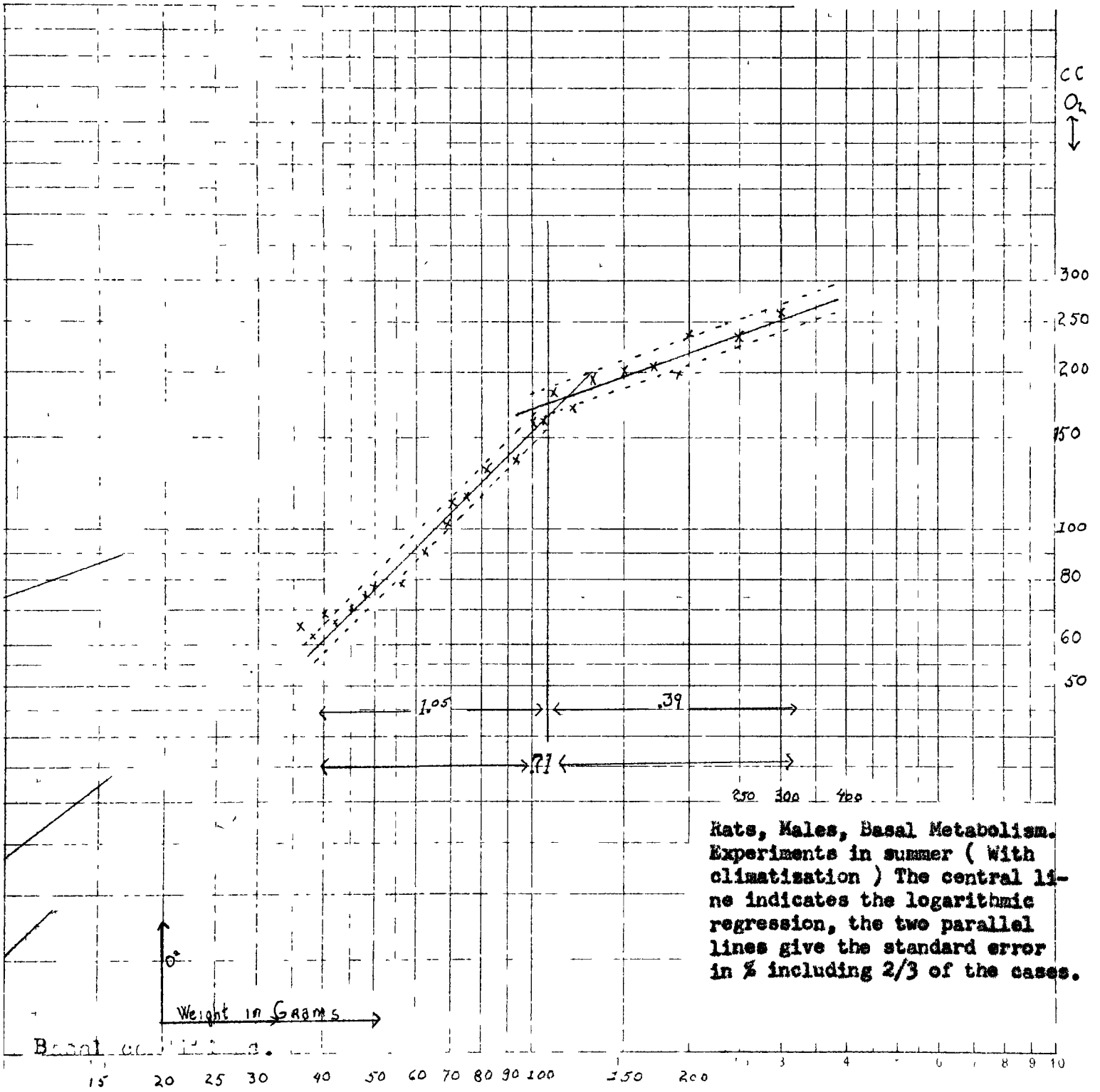


Rats, females, Basal Metabolism Experiments in summer (With climatization) The central line indicates the logarithmic regression, the two parallel lines give the standard error in % including 2/3 of the cases

Figure 10

Male Rats

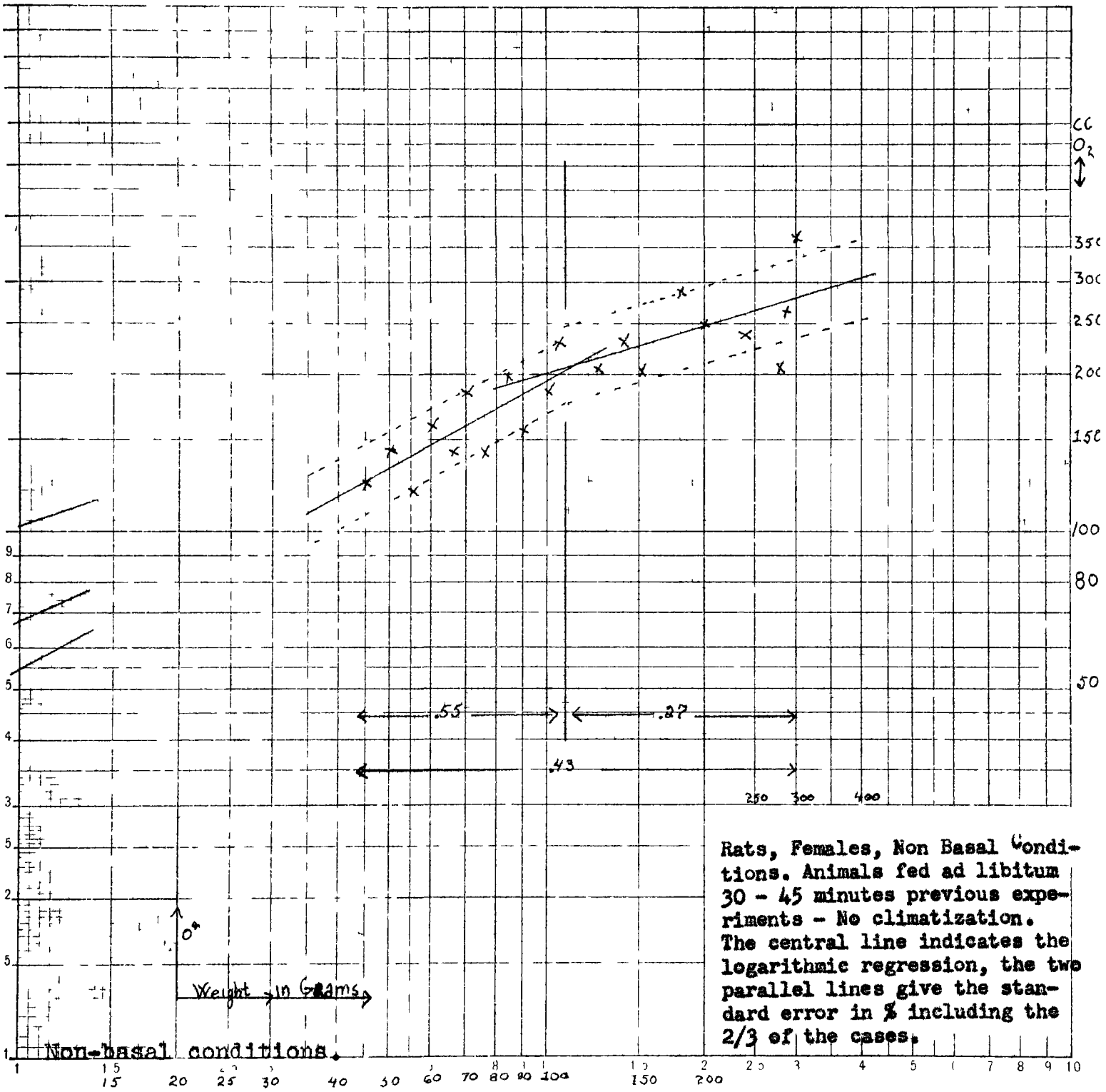
Summer Determinations



Rats, Males, Basal Metabolism. Experiments in summer (With climatization) The central line indicates the logarithmic regression, the two parallel lines give the standard error in % including 2/3 of the cases.

Figure 11

Female Rats



Rats, Females, Non Basal Conditions. Animals fed ad libitum 30 - 45 minutes previous experiments - No climatization. The central line indicates the logarithmic regression, the two parallel lines give the standard error in % including the 2/3 of the cases.

Figure 12

Male Rats

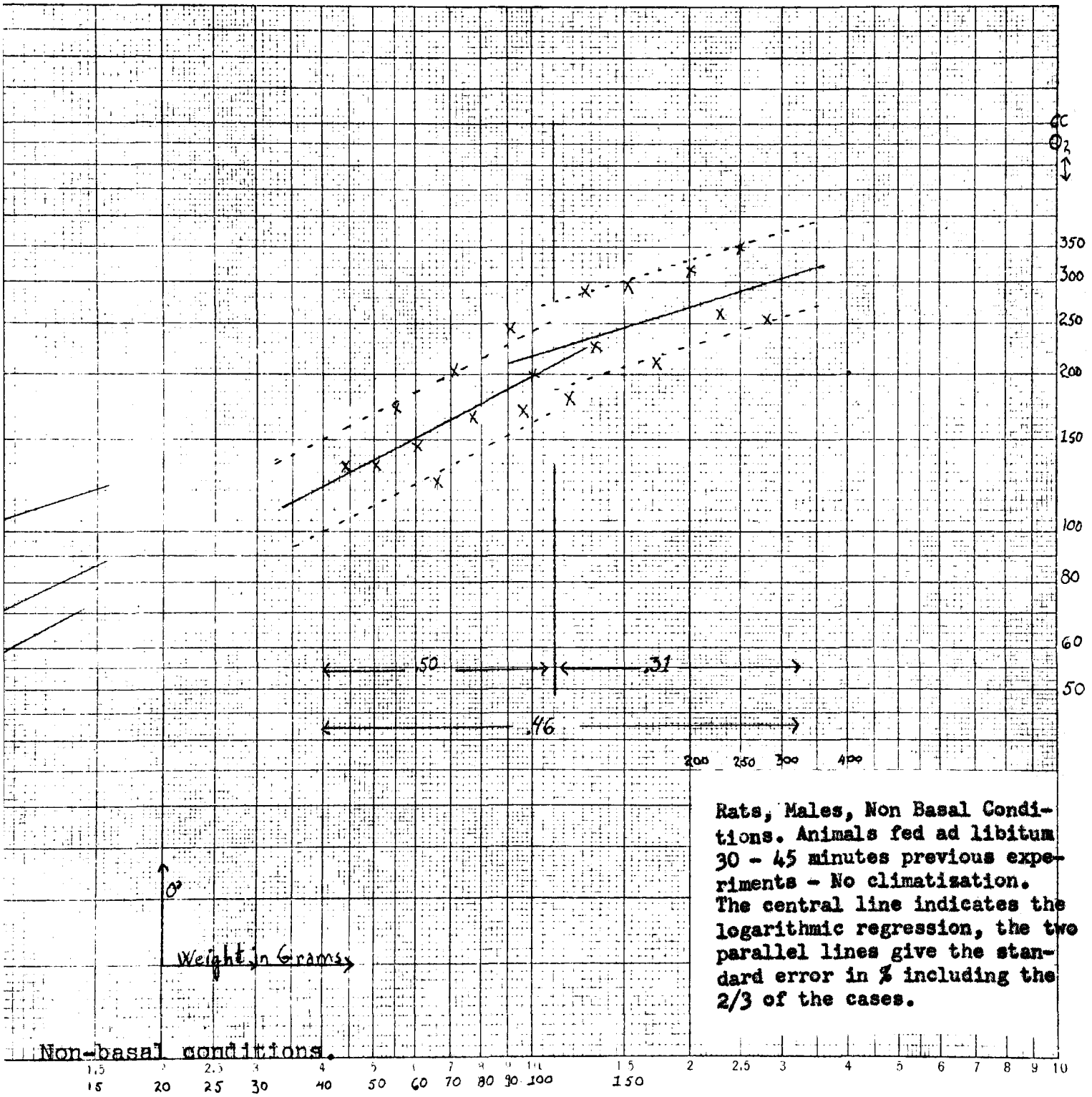


Figure 13

TABLE V

Basal conditions

FEMALE RATS (Gurner 1950)

Calculation of curves for weights of	a	b	ρ	Standard Error of Estimates +	Standard Error of Estimates −	$S_{\log y \log x}$
40 - 110 grams	1.07	16.8	.9597	13.5	11.9	.0550
110 - 300 grams	.367	78.2	.8937	18.9	15.8	.0752
40 - 300 grams	.65	36.8	.8956	30.	25.1	.1140

MALE RATS

40 - 110 grams	1.05	15.2	.9836	10	8.1	.0414
110 - 300 grams	.39	74.2	.8969	10.5	9.5	.0433
40 - 300 grams	.71	25.3	.9279	25.3	19.5	.0944

TABLE VI

Basal Conditions

FEMALE RATS (Winter 1950)

Calculation of curves for weights of	a	b	ρ	Standard Error of Estimates +	Standard Error of Estimates −	$S_{\log y \log x}$
40 - 110 grams	.92	23.0	.9557	12	10.7	.0490
110 - 300 grams	.33	83.0	.8346	16	14.	.0640
40 - 300 grams	.57	35.0	.8881	30	23.1	.1130

MALE RATS

40 - 110 grams	.943	19.0	.9798	11.	10	.0450
110 - 300 grams	.32	98.4	.9480	7	6.6	.0290
40 - 300 grams	.610	34.7	.9276	23	18.7	.0899

TABLE V11

Non Basal Conditions

FEMALE RATS

Calculation of curves for weights of	a	b	ρ	Standard Error of Estimates +	Standard Error of Estimates −	$S_{\log y \log x}$
40 - 110 grams	.552	53.0	.6596	42	29.5	.1522
110 - 300 grams	.274	102.	.2625	53.5	34.8	.1861
40 - 300 grams	.431	66.2	.7963	79.	44.2	.2528

MALE RATS

40 - 110 grams	.497	60.0	.4570	62	38	.2095
110 - 300 grams	.311	106.	.2175	70.7	41.4	.2322
40 - 300 grams	.460	71.8	.6986	70.5	41.	.2317

Theoretical representation of the shift in Metabolism under varying conditions. (Regression Lines).

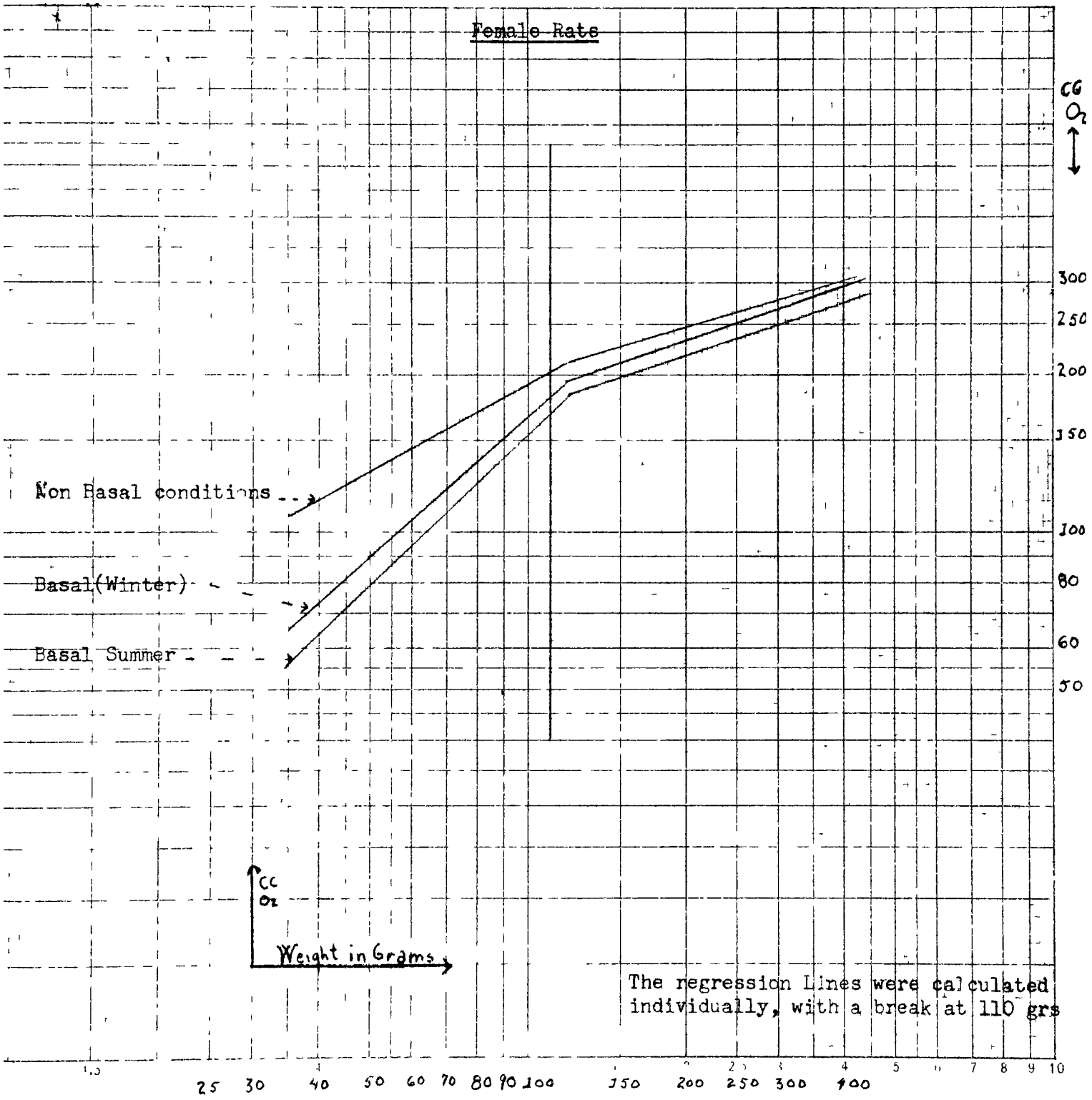


Figure 14

Theoretical representation of the shift in Metabolism
under varying conditions (Regression Lines).

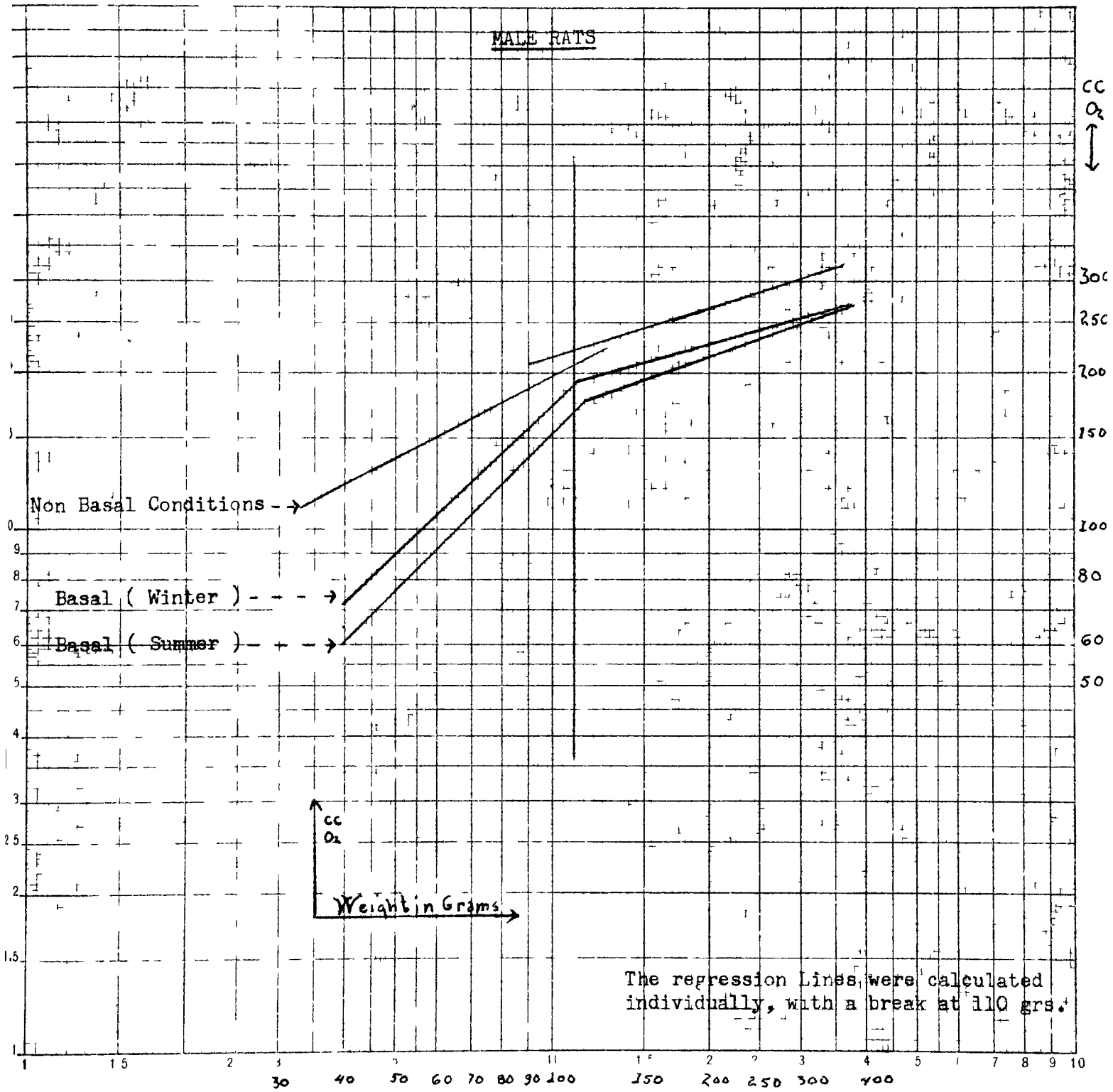


Figure 15

TABLE V111

Theoretical values of O_2 consumption under different conditions, calculated from the regression lines.

Weight in grams	Basal Conditions				Non-basal Conditions	
	Summer		Winter			
	Males	Females	Males	Females	Males	Females
30	46 cc	48 cc	55 cc	56 cc	105 cc	95cc
40	60	64	72	74	124	115
50	76	80	90	90	140	132
60	92	95	106	104	153	145
70	107	110	122	120	165	160
80	123	125	140	135	176	168
90	133	140	155	152	190	182
100	152	154	172	165	200	194
125	185	186	200	190	235	215
150	196	200	210	210	246	228
175	210	210	220	220	260	240
200	218	218	236	230	270	250
225	225	225	237	240	280	258
250	235	235	245	245	290	265
275	240	240	250	255	300	272
300	250	250	258	263	310	282
325	258	258	265	270	318	288

TABLE IX

RANGE OF VARIATION IN O_2 CONSUMPTION

Summer Results

Females		Males	
Body weight in grams	Range of O_2 variations	Body weight in grams	Range of O_2 variations
28	53 - 57 cc O_2	36	58 - 72 cc O_2
30	55 - 60	38	55 - 68
32	55 - 65	40	60 - 74
35	58 - 62	44	62 - 69
39.5	60 - 70	45	60 - 74
45	68 - 80		
48	70 - 92	48	72 - 78
55	76 - 84	50	74 - 86
57	83 - 92	56	74 - 87
60	89 - 98	62	85 - 105
69.5	91 - 112	68	95 - 116
76	104 - 120	70	101 - 140
80	115 - 138	75	110 - 120
90	119 - 140	81	117 - 139
95	142 - 166	93	124 - 140
99	165 - 178	100	149 - 176
105	153 - 174	105	151 - 168
		110	170 - 189
113	178 - 220		
120	154 - 180	120	162 - 198
126	200 - 240	131	185 - 230
130	170 - 190	149	190 - 215
145	210 - 250	170	189 - 215
150	185 - 205	190	190 - 210
170	180 - 210	250	215 - 265
176	205 - 255	300	246 - 280
190	195 - 208		
200	189 - 260		
220	189 - 240		
250	215 - 270		
298	245 - 270		
330	240 - 300		
348	264 - 320		

TABLE X

RANGE OF VARIATION IN O_2 CONSUMPTION

Winter Results

Females		Males	
Body Weight in grams	Range of O_2 variations	Body Weight in grams	Range of O_2 variations
30	58 - 70 cc O_2	37	76 - 84 cc O_2
37	68 - 75	38	75 - 88
39	70 - 80	39	73 - 80
43	77 - 86	41	80 - 90
44.5	76 - 90	47	82 - 100
46.5	79 - 91		
		50	88 - 103
53	84 - 96	54	93 - 106
56.5	94 - 108	59	95 - 108
62	103 - 125	64	98 - 117
71	98 - 122	70	110 - 122
74	118 - 130	74	122 - 142
80	128 - 150	80	138 - 160
91	144 - 164	91	135 - 160
96	155 - 185	100	148 - 180
105	149 - 185	105	175 - 195
110	165 - 205		
		111	180 - 196
120	175 - 200	121	175 - 200
134	165 - 190	136	183 - 210
126	195 - 220	150	190 - 218
151	210 - 250	161	196 - 225
161	185 - 200	180	205 - 228
179	185 - 215	200	208 - 235
185	218 - 245	238	215 - 245
200	215 - 244	251	230 - 265
205	195 - 230	262	240 - 275
246	212 - 235		
250	235 - 255		
275	242 - 275		
297	254 - 286		

TABLE XI

RANGE OF VARIATION IN O_2 CONSUMPTION

Non Basal Conditions

Females		Males	
Body weight in grams	Range of O_2 variations	Body weight in grams	Range of O_2 variations
45	115 - 130 cc O_2	43	120 - 160 cc O_2
50	125 - 150	50	125 - 150
55	100 - 140	55	158 - 180
60	148 - 168	60	120 - 170
66	128 - 145	64	115 - 135
70	170 - 196	71	190 - 220
76	124 - 153	77	150 - 200
89	144 - 165	90	200 - 280
101	175 - 200	96	155 - 210
106	200 - 250	100	186 - 215
125	185 - 240	117	170 - 194
140	220 - 240	126	275 - 310
151	175 - 225	131	215 - 240
181	275 - 300	151	275 - 325
239	225 - 250	200	300 - 330
200	220 - 270	171	195 - 225
280	190 - 220	231	245 - 280
285	245 - 280	250	320 - 370
301	340 - 385	281	220 - 310

Table VII

Comparison of Basal Metabolism in Rats as determined by different authors.

Authors	Weight of animals in grams	Calories per day	Cc O_2 per hour (1)
Davies	150	25.6	227 - 275
Benedict	150	17 (2)	150
Brody (2)	150	32.8 (3)	250
Smit	200	22.5	198
Field & al	150	18.5	164.5
Carr (3)	170	24.5	217.6
Sherwood	151 Males:	21.0	187.
	Females:	20.5	181.5
Müller and Bortalaffy	150 Males:	28.4	250
	148 Females:	29.3	265
Present work	150 Males:	22.5	200
	150 Females:	21.8	194

1 - Cc O_2 per hour were changed to calories and vice-versa on the basis of 4.7 calories = 1 liter of oxygen in fasted animals (rats).

2 - No allowance made for diurnal cycle.

3 - Allowances made for diurnal cycle.

BASAL METABOLISM IN RATS

Unpublished experiments by Müller and Bertalanffy.

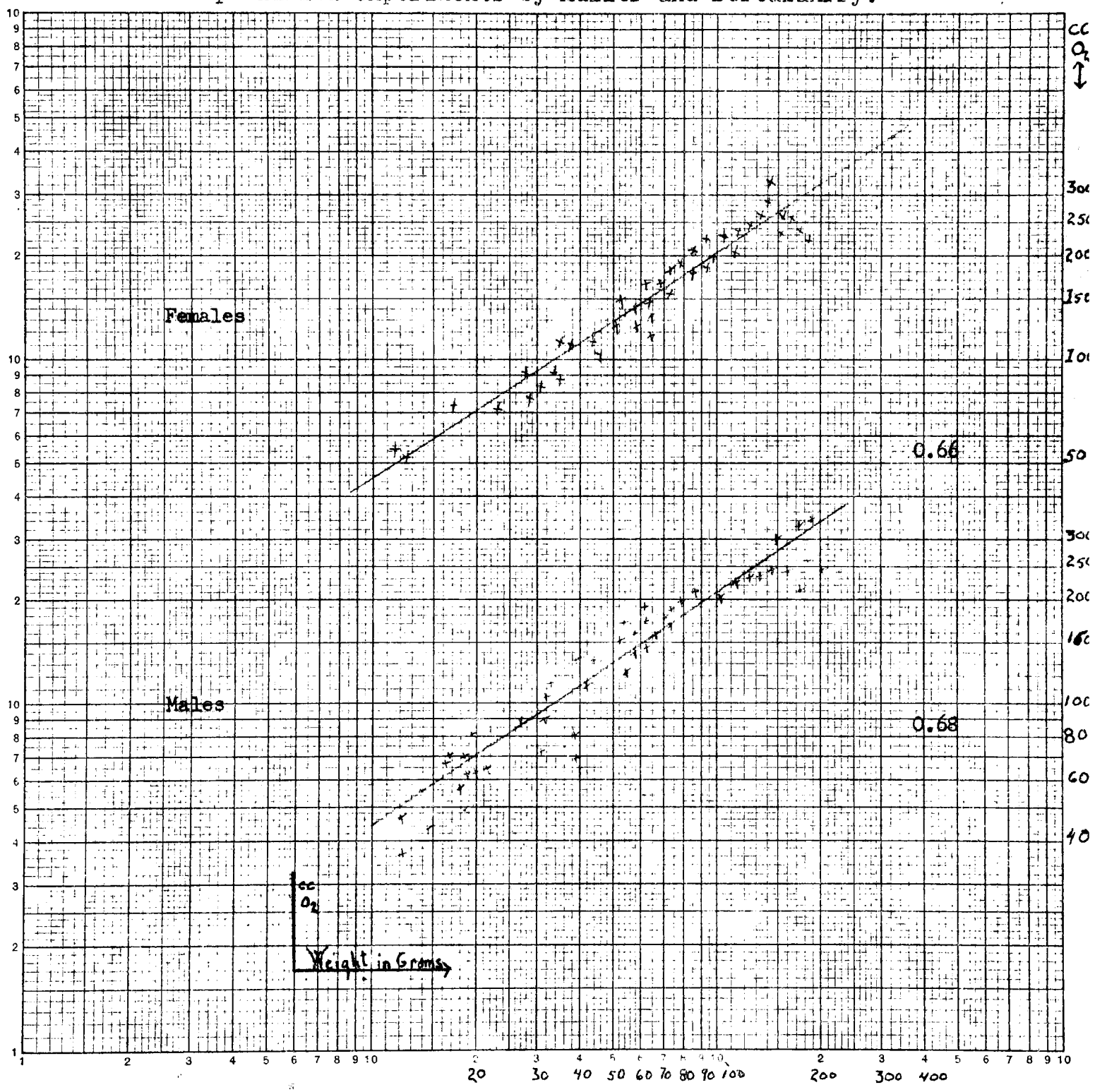


Figure 16

These experiments were done at the University of Vienna.

TABLE XIII

Basal Metabolism of " Slow Growth " Rats. (1)

Number of rats	Age Range (days)	Average Weight	Average calories per 200 gram.	CC O_2 per hr.
7	42 - 45	83 grams	36.5	133
11	56 - 70	119	30.6	160
12	71 - 85	140	27.6	170
14	87 - 99	175	25.8	196
7	101- 126	218	23.2	223
17	131 - 148	248	21.3	232
8	170 - 226	341	18.6	277
13	232 - 302	359	18.8	296

1 - Horst & al, 1934.

Mice, Basal Metabolism.

The results are indicated in Tables XlV, XVl and Figure 16 (pp. 68 - 70). Male mice follow rather closely the surface rule (α = 0.68) while female mice show a much steeper slope (α = 0.88). This may, in some way, be connected with the fact that pregnant animals were not excluded from the experiments.

If we consider the absolute values of our experiments compared to those of other investigators, we find that Benedict (1938) obtained for animals of approximately 25 grams, 4 to 5 calories per day as basal metabolism, while Ebeling and Corey (1) although in the same range of values had results slightly higher than Benedict's (See Figure 2b, p. 13). From the results shown in Table XlV, (P. 68) we see that an animal of 24 grams gave, for the sake of comparison, on a per diem calculation, 4.9 calories, although this method of calculation was not used. For 30 grams animals our values exceeds slightly those of Benedict (1938) being close to 6.8 calories for females and 6 calories per day for males. If however, the lowest values are used for the computation, instead of averages, our results are very close and not in excess to Benedict's (1938) although our computation becomes more difficult because of the dispersion of the data.

Mice, 21° C.

In an environment which is not thermoneutral, the abso-

---

1 - Results published with Benedict's (1938) (Same paper)

lute values of O_2 consumption are, of course, higher than under thermoneutrality, owing to the energy expense for thermoregulation, thus, under basal metabolism conditions, 35.6 cc and 49 cc O_2 per hour were consumed at a temperature of 29° - 31° C. by animals of 17 grams and 30 grams body weight respectively, while at 21° C. the same animals took respectively 109 cc and 145 cc per hour, which values are slightly in excess to the ones found by Hart (1950b).

As the increase in Oxygen uptake is taking place , the slope of the allometric becomes significantly smaller: α = 0.68 at 29° - 31° C. temperature and α = 0.60 at 21° C. (Table XVI Figures 17 and 19 (pp.69 and73).

Mice, Running.

The results for running animals are very scattered due to the fact that it is hardly possible to control the experiment completely. The large oxygen consumption is obvious: under basal metabolism conditions, animals of 20 grams and 26 grams took respectively 40 cc and 49 cc per hour while animals of 18 grams and 25 grams consumed respectively 140 cc and 165 cc O_2 per hour while running. Again it appears that the slope of the allometric line is decreased (α = 0.60 at rest and α = 0.52 when running at controlled speed) (Figure 19b p73). Owing to the scattering of the points the figures for α i n the experiments with exercise are to be considered as a qualitative indication for the body size-metabolism

relation, rather than in their numerical values. As seen in Table XVI, the ρ values are very low, indicating that under conditions of activity not body size is the main factor in controlling metabolic rate, but rather the work done (running speed, etc) factors which were not completely controlled in the present preliminary experiments. Body size, while being a predominant factor in metabolic rate under basal conditions (and also under non-basal conditions of thermoregulation in non-thermoneutral environment) is a factor of only secondary importance under conditions of muscular exercise.

Dealing with groups of 4 mice having average body weight of 26.72 grams, Hart has studied the Oxygen consumption under different conditions. (Figure 18b, p.72). This group can be compared to running mice, trained, running at controlled speed as shown in Figure 19b, (p.73) although we made no differences between light and moderate work.

When comparing the O_2 consumption of running animals in relation to body weight, the main problem consists in finding the particular speeds at which small and large animals should run to do the same approximate work. The difficulty of solving this problem resides in the fact that smaller animals run better than larger ones. We thus have to consider the factor of training for large animals. (1)

---

1 - The training consisted of 4 to 5 periods of running from 10 to 20 minutes each given during the evening. Large animals who could not run or could not reasonably increase their speed were rejected.

1) Without training: If we run the animals at 15 cm per second, the larger animals cannot maintain this speed and will soon ride the cage while smaller animals, though they can run that speed, soon show signs of fatigue. They can be both, small and large animals, considered as working heavily at that speed, and the oxygen consumption in such cases is shown in Table XV, (p.70) and Figure 19a (p.73), giving a slope of $a = 0.262$ as compared to $a = 0.68$ at rest (under B.M.).

2) With training: If all animals are given a few training exercises, trying to speed up the larger animals and slow down the smaller ones, we see that small animals can easily take a speed of 10 to 12 cm per second while larger ones can be made to follow the cage easily enough at 12 to 14 cm/sec. Then the O_2 consumption becomes as shown in Figure 19b (p.73) the slope of the allometric line being $a = 0.523$.

It does not seem that further slowing down of smaller animals or speed increase for larger ones will re-establish the original slope. In fact it seems as if further training would have made the animals all run at the same speed, medium weight animals being best while small and large ones were first tired.

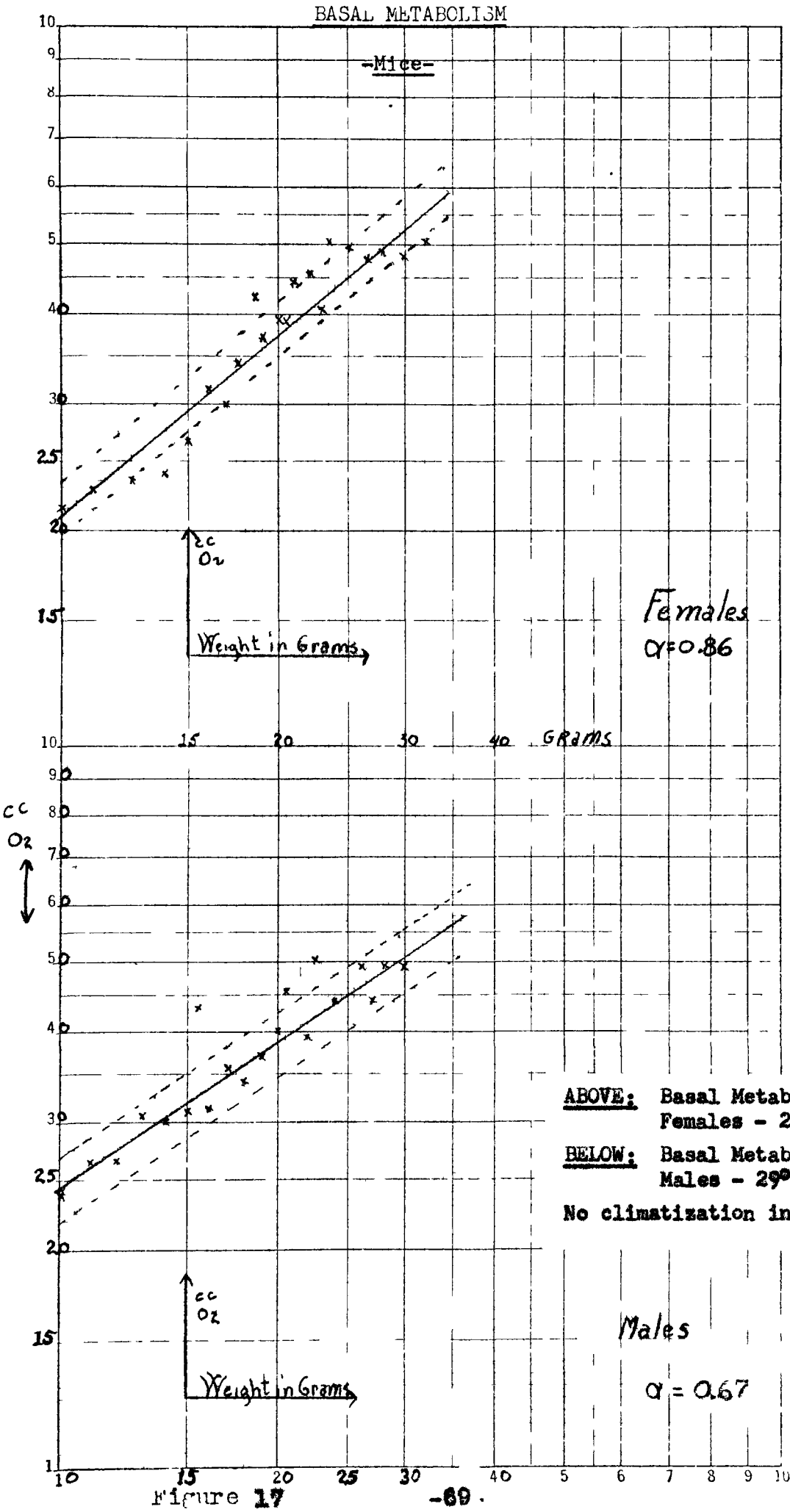
It is to be noted that the animals were left running about 5 to 10 minutes before any determinations were done.

TABLE XlV

Results - Mice

Basal Conditions

Males		Females	
Body Weight in grams	Cc O_2 / hr Average of three lowest experiments	Body Weight in grams	Cc O_2 / hr Average of three lowest experiments
10	24 cc O_2	10	22 cc O_2
11	26.6	11	22.7
12	26.8	12.5	23.8
13	30.3	14	24.1
14	30	15	26.6
15	30.6	16	31.6
15.5	43.3	17	30.3
16	31.6	17.5	34.3
17	35.6	18.5	37
18	34	18.5	42
19	37	20	39.6
20	40	20.5	39.6
20.5	45.3	21	44.3
22	39.3	22	45.6
22.5	50.3	23	41.6
24	44.3	23.5	50.6
26	49.6	25	49.3
27	44.6	26.5	47.6
28	49.6	28	48.5
30	49	30	48.3
		32	51.1



ABOVE: Basal Metabolism - Mice
Females - 29° - 32° C.

BELOW: Basal Metabolism - Mice
Males - 29° - 32° C.

No climatization in either case.

Figure 17

TABLE XV

Non Basal Conditions

At 21° C.		Running (trained)		Running (untrained)	
Body Weight in grams	cc O_2 pr/hr	Body Weight in grams	cc O_2 pr/hr	Body Weight in grams	cc O_2 pr/hr
17.5	109.6	16	138	13	125
19.8	123.7	17.5	129	15	140
21.7	123.7	18	146	15.3	146
21.9	128.6	19.1	141	15.6	154
22.6	135.7	19.3	106	17	170
24	137.8	22.1	188.6	180	150
25.2	133.6	24.9	180	20	144
25.8	138.5	25	176	20.3	192
27	147	25.3	159.5	22	180
32	151.8	26	142	23.4	170
35	177.1	32.5	187.4	26.5	165
				26.8	200
				28	185

TABLE XVI

RESULTS - MICE

Basal Conditions

	a	b	ρ	Standard Error of estimates +	Standard Error of estimates -	$S_{\log x \log y}$
Males	0.676	24.2	.8575	9.5	8.6	.0393
Females	0.86	21.0	.8751	11.	9.93	.0454

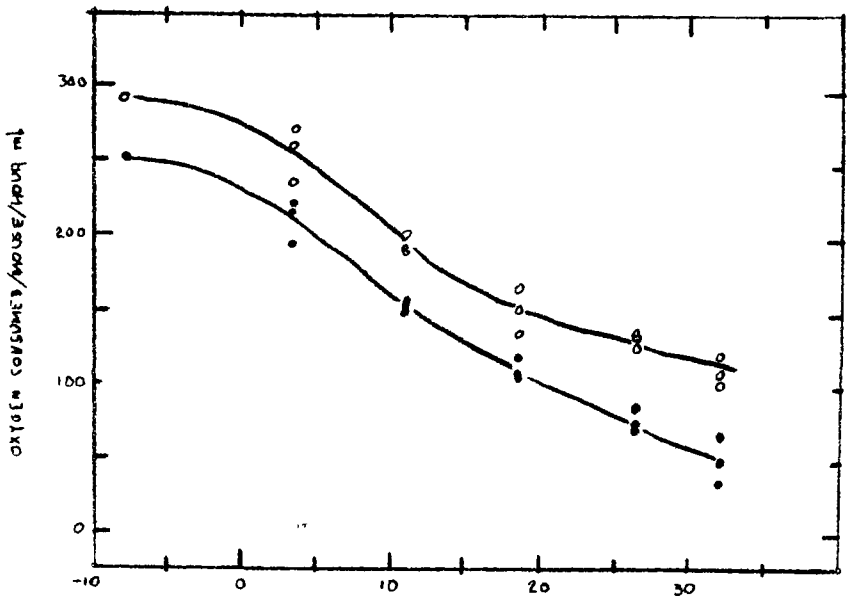
Non Basal Conditions

Males

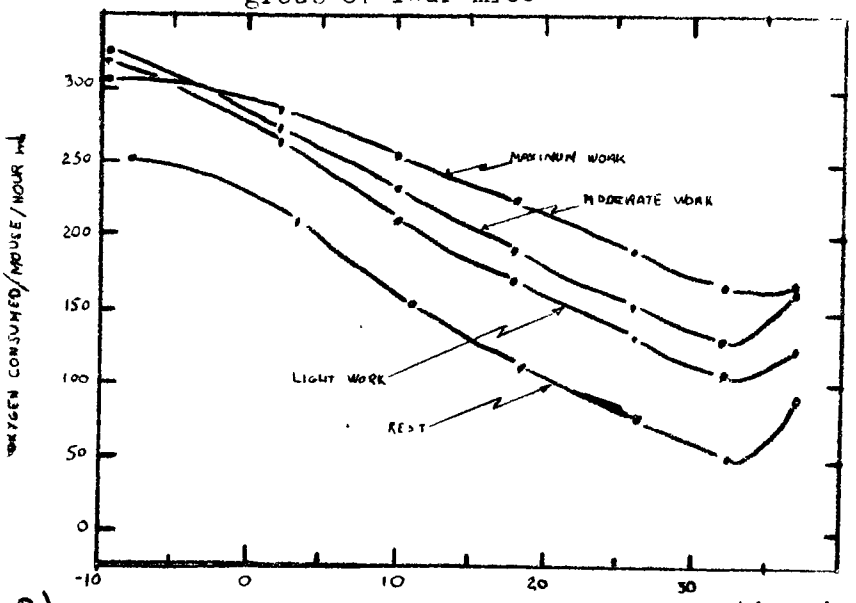
21° C.	.6012	80.21	.9315	3.48	3.43	.0148
Running. (No training)	.262	102.3	.2362	17.6	14.7	.0704
Running. (With training)	.5238	100.5	.3162	15.3	13.2	.0618

Figure

18



A) Minimal (●) Maximal(o) oxygen consumption in daily metabolic cycle in relation to temperature for each group of four mice



B) Effect of temperature upon oxygen consumption during rest, light work (speed 4.25 cm/sec) moderate work (speed 9.9 cm/sec) and maximum work. Data for rest are averages of lowest values in daily cycle except at 37o C. where they are average of lowest values in tests lasting three to five hours.

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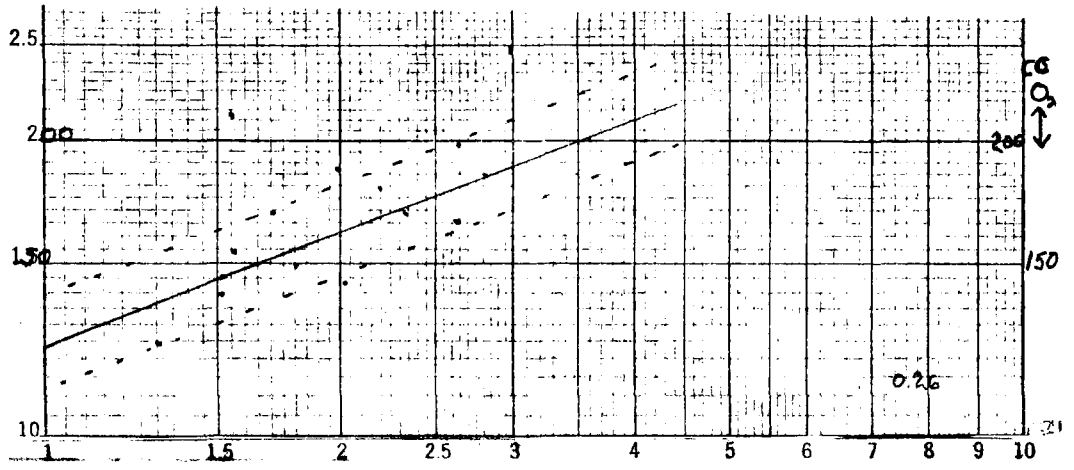
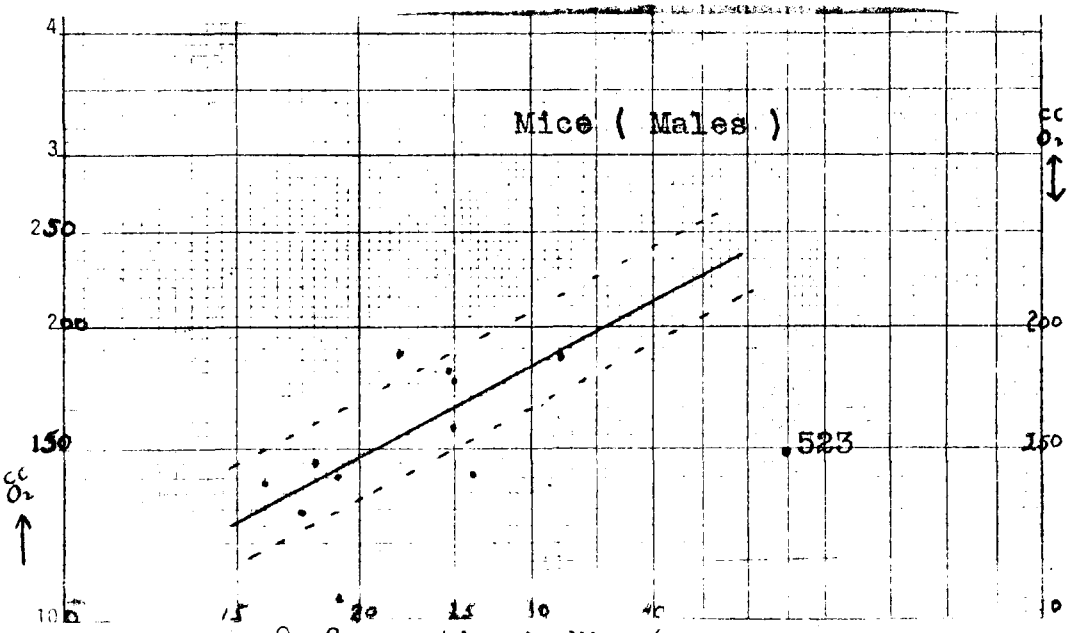
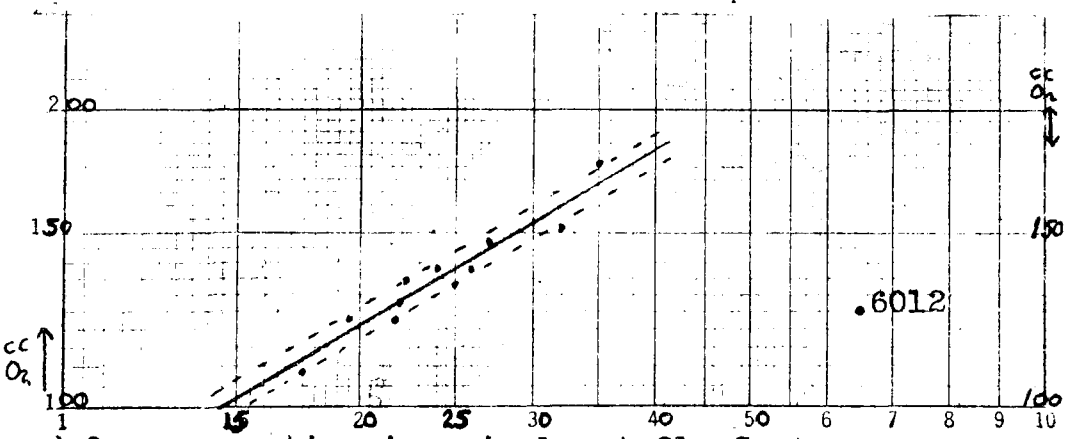
Hart J.S.



A) O_2 Consumption in Mice (Males, untrained)
Running at Maximum speed
(Maximum speed of each animal)



c) O_2 Consumption in Mice (Males, trained)
Running at controlled speed



c) O_2 consumption in animals at 21o Cent

Figure 19

Note: The plain line indicates the logarithmic regression, dotted lines give the standard error in % including 2/3 of the cases.

CHAPTER V

DISCUSSION

From the material presented here, the following conclusions can be drawn:

1) The relation between metabolism and body size varies under different metabolic conditions. The slope of the logarithmic regression line indicating the relation of metabolism and body size is highest under basal conditions and decreases successively for conditions of non-fasting, non-thermoneutral environment and muscular exercise. The fact that small animals are more versatile to external changes and their metabolism can undergo greater and quicker changes than larger animals when submitted to varying conditions seems to be the best explanation for the shift of the allometric line. On the other hand, genetic and environmental factors retarding growth seems to lead to a smaller slope of the regression line, as is the case in Müller's and Horst's experiments (p. 62 and 63. Table XIII and Figure 16)

2) The surface rule ($\alpha = 2/3$) applies:

   a) to rats, males and females, under basal conditions, as a gross approximation over the whole range of weight.

   b) to mice, males, under basal conditions; in females, pre-

gnancy is possibly the reason for the deviation from the surface rule.

The surface rule (Q = 2/3) does not apply to the relation between basal metabolism and body size in rats in detail, the first part of the curve being considerably steeper and the second more level than a solution according to the surface law.

3) In growing rats, a break in the metabolism-body size curve is found in both sexes. This break, dividing the allometric line into two sections and taking place at about 110 - 120 grams body weight, is sharp under basal conditions and less marked (probably not existant) under non-basal conditions of resting metabolism.

   There seems to be no doubt that at this size, corresponding to the time of beginning of puberty, a deep-reaching metabolic change takes place in rats. It manifests itself in several different and independently investigated phenomena:

   a) The change in metabolism. This change is quite noticeable as reported by Brody (Figure 3, p. 14) and as found in this study and illustrated in Figures 8, 9, 10 and 11 (p. 46 - 49)

   b) Growth curves, as found in the calculation of Growth of the white rat and mice. Absolute and relative growth show a decrease and subsequent increase in the period in question (in rats, ca 100 gm. body weight) Accordingly, there is a change in the constants of the growth equation

calculated according to formula 9 (below). The growth for length and weight (data from Donaldson, calculated by Bertalanffy) are shown in Figure 21 where the cycles of the growth curves may be seen.

c) Relative growth of the liver. Similar to the general growth curve of the rat, the relative growth of the liver shows a " periodization " in its development (Figure 20, p. 80) (Bertalanffy and Pyrozinski, 1952.)

d) Growth of thymus. The growth curve of this organ also is " periodized ", maximum development being attained at approximately 100 grams body weight before involution begins. (Bertalanffy and Pyrozinski, 1952.)

e) Tissue respiration. In a study on tissue respiration Bertalanffy and Pyrozinski (in press) reported as follows: Apart from the thymus, the liver is the only one among the organs studied to show in the allometric curve of Q_{O_2} occurring at about 100 gram body weight.

4) Some remarks may be made as to the connection between metabolism and growth according to Bertalanffy's comprehensive theory of growth. This theory is based upon the assumption that growth may be considered the result of building up and breaking down, anabolism and catabolism of building materials as expressed by:

$$\frac{dy}{dt} = \lambda y^m - \chi y^n \qquad (9)$$

where λ and $\varkappa$ are constants of anabolism and catabolism respectively and the exponents m and n indicate that the latter are proportional to some powers of body weight y. It appears that it is possible to establish a strict connection between growth types and metabolic types and examples on each of these types was given on page 3 (Bertalanffy, 1951.)

As far as growth in mammals is concerned, Bertalanffy has emphasized the complexity of this phenomenon. He has, in particular, stressed the fact that, as contrasted with simpler cases of growth, the growth curve in mammals is sub-divided into " cycles " which can be seen distinctly in mice and rat and are most marked in the growth curve of man. These cycles into which the growth curve is sub-divided are not arbitrarily assumed as is the case with the sub-division of the growth curve into sections for the purpose of fitting the curve to a certain mathematical formula as done by many authors; they are objectively characterized by a decrease and subsequent increase of growth rates (Bertalanffy, 1938.) and correspond to fundamental changes in the hormonal balance, especially in puberty.

Under the assumption that mammals belong to the " First " metabolic and growth type " (surface rule of metabolism) Bertalanffy, 1938, 1951a) has given a detailed analysis of growth in the albino rat (Data of Donaldson), the male mouse (data of Stieve) and man.

He was able to show that assuming two cycles of growth the growth curves of rat (Figure 21, p. 80) and mouse can be calculated with good fit and accounting for all details, by means of the growth formulae deduced from theory, in much better approximation indeed than by other, often much more complicated and physiologically meaningless growth formulae. It cannot be emphasized too strongly, however, that these calculations are considered by Bertalanffy more as illustrations for his theory than as inexorable " laws " of growth for the species in question, which justly can be doubted for so complex a phenomenon

Actually, almost every worker in this field has tried to represent the classical Donaldson data by means of a particular formula, supposedly inapplicable to other sets of data. It appears that the growth curve in rats is highly dependent on the experimental conditions and nutrition standards (Zucker, 1941, Figure 22, p.81). Different growth curves can be obtained under different regime so that the formulae fitting one experiment do not apply to other experiments (Dunn et al, 1947). This corresponds to what was said above about the dependence of metabolism-size relation on different conditions.

Bearing in mind these qualifications, it appears that Bertalanffy's conception is applicable to mammelian growth , although only in the way of a schematization of a highly complicated process. The following relevant points can be made with respect to the results presented in this paper:

1) Bertalanffy assumes that growth in the mammals under

investigation, belongs to the " First type " in which the surface rule applies to growing individuals of different size. This according to the present results is correct with respect to the general trend of the relation of basal metabolism to body size in rats, although, in detail, the slope of the first part is greater and of the second part is smaller than $\alpha = 2/3$. Under non-basal conditions, it is found that $\alpha < 2/3$, which, however would not essentially alter the general shape of the growth curve (1) only the point of inflexion being shifted. In male mice, α also is $\sim$ 2/3 under basal conditions and somewhat less under non-basal conditions.

---

1 - If, in the first type, $\frac{dy}{dt} = \eta y^{2/3} - \chi y$ (9)
the point of inflexion is calculated as follows:
Equating (1) to zero, we have,

$$\eta = \chi Y^{1/3} \qquad (Y = \text{final weight})$$

Hence $\frac{dy}{dt} = \chi Y^{1/3} y^{2/3} - \chi y,$

$$\frac{d^2y}{dt^2} = 2/3 \chi Y^{1/3} y^{-1/3} - \chi = 0$$

and therefore we find the point of inflexion:

$$y^{*1/3} = 2/3 Y^{1/3}$$

$$y^* = 8/27 Y$$

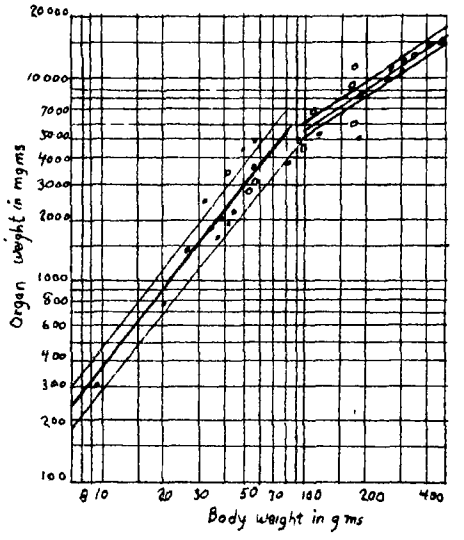


Figure 20
Relative growth of the liver in albino rats.
o = males, ● = females.

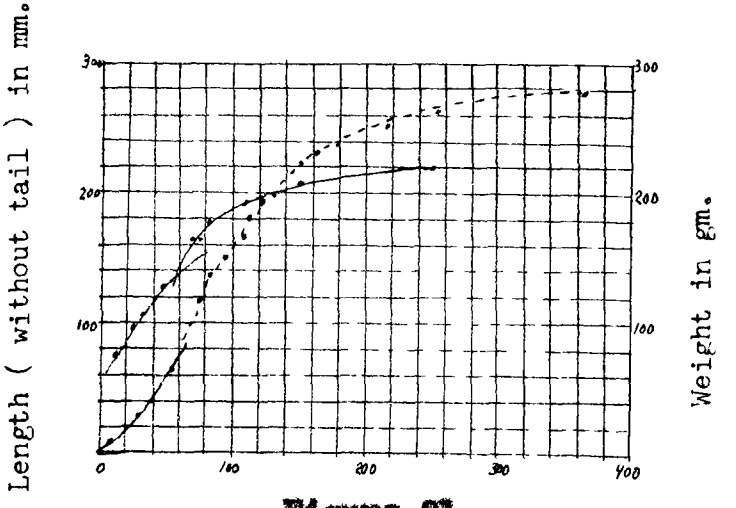


Figure 21

Heavy curve = Length growth.
Broken curve = Growth inWeight.

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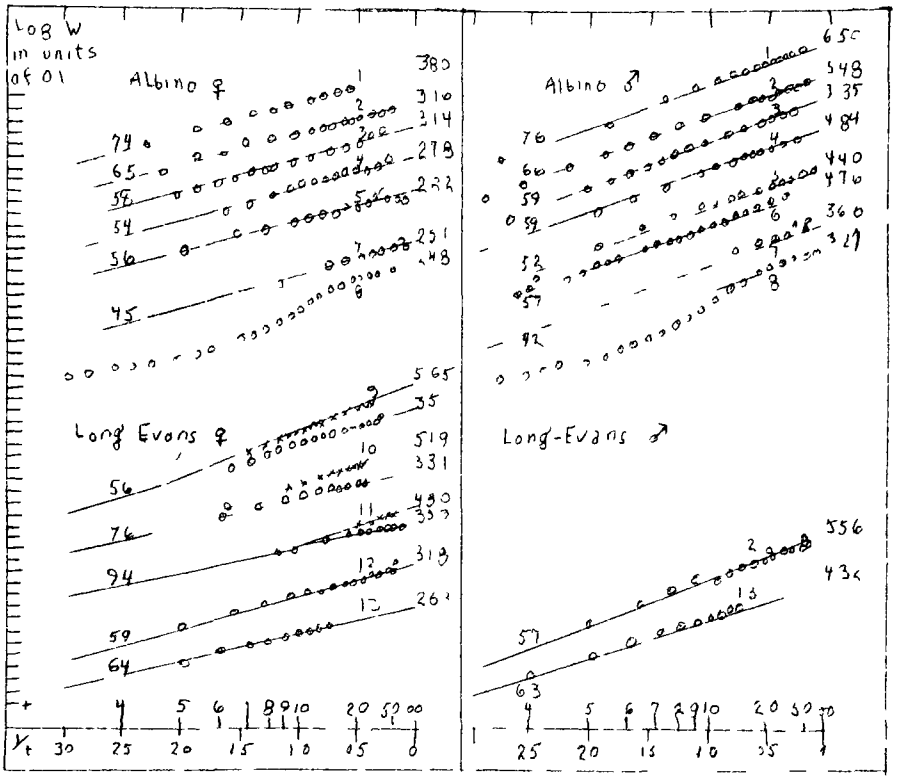
Table 9 - p. 527, 1941.

Figure 22



Log reciprocal plot of the growth of various rat colonies on diet optimal for growth.
1, Mendel and Mitchell, 1935. 2, Smith and King, 1928. 3, Maynard 1930, 4, Macy et al 1927, 5, Freudenberger 1932, 6 Sherry and Stoyanoff, 1934, 7, King, 1915. 8, Donaldson et al, 1906. 9 and 10, Evans. 11, Hart and Cole, 1939. 12, Freudenberger and Evans, 1932.

If $\eta < 2/3$, for example $\frac{1}{2}$, it follows correspondingly:

$$\frac{dY}{dt} = \eta y^{1/2} - \chi y$$

$$\eta = \chi Y^{1/2}$$

$$\frac{dY}{dt} = \chi Y^{1/2} y^{1/2} - \chi y$$

$$\frac{d^2Y}{dt^2} = \tfrac{1}{2}\chi Y^{\frac{1}{2}} y^{-\frac{1}{2}} - \chi = 0$$

$$y^* = \tfrac{1}{2} Y^{\frac{1}{2}}$$

$$y^* = \tfrac{1}{2} Y$$

Thus a value of $\eta < 2/3$ shifts the point of inflexion of the curve, but does not alter its general sigmoid shape.

2) In Bertalanffy's calculation of the growth in rats, a growth cycle is supposed which is shown by the decrease and subsequent increase of growth rates. According to theory, this growth cycle should correspond to a metabolic cycle, i.e., a change in the metabolism-size relation. The break should be at about 100 gram body weight according to the calculation of the growth curve (according to equation (9) Bertalanffy, 1938.) This is verified by the present results.

3) According to theory, there should be a correspondence between the ratio of the η's (constants of anabolism in different growth curves) and that of the metabolic rates in different groups of animals under comparison. This was verified in the case of the Guppy (lebistes reticulatus). This small fish shows marked sexual difference in the growth curves, the values of η, as calculated from the latter, standing in a relation of 1 : $1\frac{1}{2}$ for females and males respectively. Corresponding to theory, the same ratio 1 : $1\frac{1}{2}$ was found in the metabolic rates of females and males (Bertalanffy, 1941. Bertalanffy and Müller, 1943) The material presented here offers a similar comparison. From the growth equation: $\frac{dy}{dt} = \eta y^{2/3} - \kappa y$

follows that $\eta = Y^{1/3}$ with Y = Final weight

According to the calculations made by Bertalanffy (1938) for male mice (second cycle) and albino rats (first cycle) the following results were obtained:

$$\eta_{\text{week}} = 1.04 \quad (\text{p.296})$$
$$\eta_{\text{week}} = 1.58 \quad (\text{p.297})$$

for mice and rat respectively.

The ratio between the η values of mouse and rat is therefore approximately 1 : 1.5 . According to theory, it is expected therefore that a rat has a somewhat higher metabolic rate than a mouse of the same size. This is actually found since the basal metabolic rate of a male mouse of 30 grams is approximately 49 cc O_2/hr and of a male rat of the same weight, approximately 55 - 60 cc O_2/hr.

Thus the results of the present investigation suggest that Bertalanffy's conceptions are essentially correct if only as a schematic picture. Though possible, it would be rather futile to re-calculate the different growth curves as offered by a good number of investigators, taking into account the details of the metabolism-size curve and introducing them into the growth formulae mentionnd. Considering the variations in the growth curves as well as in the metabolic curves under different conditions such curve fitting would be of little value. It seems however, that the general principle is correct as shown by the considerations given above under 1 - 3.

SUMMARY

1) The relation of metabolism to body size was studied in rats and mice, under basal and non-basal conditions.

2) A simple respirometer suitable for this purpose is described.

3) The surface rule applies to the general trend of the correlation between body size and basal metabolism in rats of both sexes. It also applies to male mice.

4) In detail, however, the allometric line (logarithmic regression line of O_2 consumption against body weight) indicating the metabolism-size relation in rats is in the first part steeper, and its second part more level than would correspond to the surface rule. The break in the curve corresponds to a body weight of about 110 - 120 grams.

5) Conditions of basal metabolism, resting metabolism, non-thermoneutral environment, slight and heavy exercise, lead to a shift in the metabolism-size relation, the slope of the allometric line of O_2 consumption against weight decreasing in the sequence named. It appears that under basal conditions and in thermoregulation in non-thermoneutral environment the dependence of body weight is a predominant factor for metabolic rate. Under conditions of muscular activity, however, dependence on body size of metabolic rate is only a factor of secondary importance.

6) No marked differences in the metabolism of male and female rats of equal body size are found. In mice, small animals

University of Ottawa.

of equal sizes have approximately the same metabolism while the values for larger females are slightly higher than those of males of the same body weight.

7) A discussion of the results in connection with other data on metabolism and with the theory of growth is given.

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