

ORGAN WORK AND ORGAN WEIGHT*

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In 1924 Huxley (1) noted that there was frequently a constant relation between the relative rates of growth of the body and its parts, and in 1932 he assembled many examples of this constancy throughout the whole biological field (2). We have made use of this observation in examining data on the organ weights and body weights of a considerable number of albino rats that we had used as controls for experimental work.

EXPERIMENTAL

As will appear from the experimental data to be given, organ weight may fluctuate between wide limits when certain conditions are not kept constant, so it is important to specify the particular conditions under which these control animals were kept.

The food was given *ad libitum* and contained 18 per cent of protein. It was an air-dry mixture containing 10 per cent unpurified casein, 73 per cent corn meal, 10 per cent linseed meal, 2 per cent alfalfa, 3 per cent sardine oil, 1.5 per cent bone ash, and 0.5 per cent sodium chloride. The temperature of the room in which the rats were kept averaged 20°C. and was regulated to prevent any marked fall so that it was rarely less than 18°C., though on warm days it occasionally rose for a few hours appreciably above 20°C. in spite of a fan that kept a current of air constantly moving through the room. The rats were housed in groups of six in cages 17 × 12 × 12 inches. The colony came from the Slonaker strain from which the Wistar Institute colony was derived and for 12 years their ancestors had lived under conditions closely similar to those we have defined. They were all controls for experiments on the compensatory hypertrophy of the testicle, suprarenal, ovary, and kidney and had all undergone a sham operation in which these organs were exposed but not removed. The operations were performed on rats of exactly 30, 70, 110, and 220 days of age, and in each age division groups

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were killed for measurement of organ weight 2, 5, 10, 20, and 40 days after operation. When the organ weight measurements were arranged in accordance with age instead of body weight it was possible to measure the effect of operation by finding the deviation from the predicted organ weights or from smoothed curves of the testes, female suprarenal, and ovary. But with the exception of the suprarenal gland no significant deviations were found. It should be noted, however, that the duration of ether anesthesia was very short and that the operation itself was over within about 2 minutes. The experiments that will be given were car-

TABLE I

Number of rats	Males						Females					
	Body weight <i>gm.</i>	Heart <i>mg.</i>	Kidneys <i>mg.</i>	Liver* <i>mg.</i>	Supra-renals <i>mg.</i>	Testes <i>mg.</i>	Number of rats	Body weight <i>gm.</i>	Heart <i>mg.</i>	Kidneys <i>mg.</i>	Supra-renals <i>mg.</i>	Ovaries <i>mg.</i>
75	41-60	238	508	2305	13.90	358	69	41-60	240	516	14.50	21.0
69	-80	309	626		17.46	494	79	-80	298	614	17.94	24.6
54	-100	365	742		19.06	800	34	-100	363	762	22.50	31.6
46	-120	445	912		21.82	1064	32	-120	429	892	30.54	45.6
39	-140	498	1000		21.02	1364	82	-140	492	976	39.84	73.0
37	-160	554	1112		23.76	1598	134	-160	542	1068	44.74	80.6
77	-180	610	1252	7240	25.12	2024	157	-180	592	1116	48.36	87.4
79	-200	670	1350	7610	26.66	2326	127	-200	649	1222	48.74	90.2
53	-220	715	1448	8060	28.56	2416	63	-220	696	1300	48.76	84.6
56	-240	755	1492	8770	29.20	2590	20	-240	734	1370	48.70	85.2
45	-260	780	1590	8840	31.60	2654						
39	-280	841	1674	9830	32.70	2626						
51	-300	885	1774		33.36	2650						
39	-320	936	1844		34.90	2880						
36	-340	968	1900		35.26	2912						

* The liver weight measurements were made on another series of 229 rats kept under identical conditions except that there was no operation. More extensive data than we possess might reveal a sex difference in liver weight analogous to the sex difference in kidney weight but our present observations on female rat livers indicate that, if present, any such difference must be small.

ried out during the period over which these control observations were being made so that the possibility of change in the colony itself was excluded. Some of the measurements of the protein content of the liver have been already published in papers concerned with protein metabolism that are referred to in this paper, and the method used and the conditions observed are there described in detail.

The average organ weights arranged in accordance with body weight are given in Table I.

If the ratio between the rate of growth of the body and the rate of growth of any organ is constant, a plot of the logarithm of organ weight against the logarithm of body weight forms a straight line. When this is done for the data in Table I it is found that the organs fall into two classes, those whose logs fall along straight lines and those whose logs form sigmoid curves. In the latter class fall the testicle, ovary, and ♀ suprarenal, organs that for a short time during puberty undergo a marked growth acceleration. In the other organs, including those in which we are at present interested, there is an approximate constancy in the relative rates of growth of organ and body since the lines are straight. (See Figs. 1 and 2.)

The practical advantage of this straight line relationship is that it makes it easy to derive formulas with which organ weight may be predicted from body weight with considerably greater precision than is given by any of the other methods we have tried. Those made use of in this paper are given in Table II.

The slopes of the lines in Fig. 1 are determined by the method of least squares from the logarithms of the measurements given in Table I. These slopes give the ratios between the relative rates of increase of organ and body weight and are the powers of the body weight appropriate for each organ. Thus the heart weight varies as the (body weight)^{0.750}, indicating that the heart increases at 0.75 times the rate at which the body weight increases. The powers of the body weights were then calculated in numbers and the slopes of the lines obtained when the actual organ weight measurements were plotted against these numbers were determined by the method of least squares. The formula is now in the form $\text{organ weight} = a \times \text{body weight}^n \pm b$. The constant a is the slope. The constant b , as Hall (3) has pointed out, is required because an extrapolation of the line does not cross the ordinate at zero. Actual observations from the body weight at birth show that the relationships given by the formulas do not hold below a body weight of 40 gm. and in the control observations given here the smallest animals had been weaned and had subsisted wholly on the control diet for at least a week. This b constant = average organ weight - ($a \times$ average body weight). To save the time required for calculation tables giving predicted organ weights for every gram change in body weight were constructed from large graphs.

The prediction errors given in Table II are the averages of the percentage deviations, summed without respect to sign, of the weights predicted by the formulas from the means of the organ weights given in Table I. In considering the significance of the experimental

results we are to present we shall be concerned with gross deviations from the predicted values, and will discuss only those that lie beyond the range of the greatest + to the greatest - deviation of

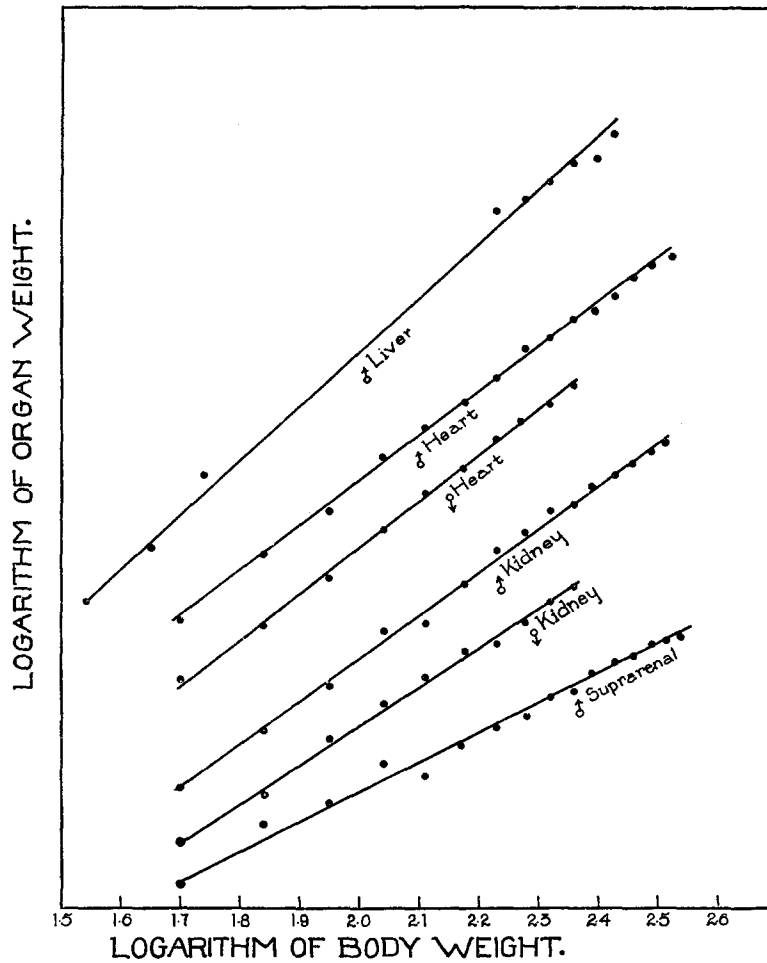


FIG. 1

any of the groups in Table I. These ranges of error are given for each formula in Table II.

The experimental results in Table III are derived from observations on groups of rats comparable with those whose organ weights are

given in Table I. They were subjected to essentially the same conditions¹ with the exception of one experimental variable. These vari-

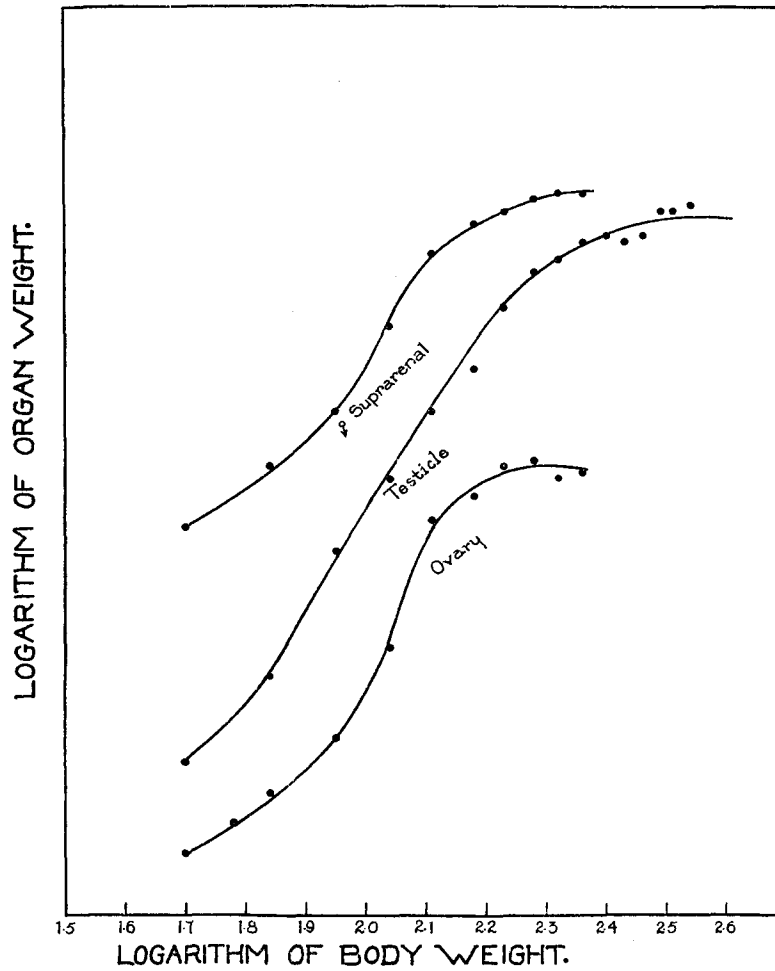


FIG. 2

¹The housing and temperature conditions were identical and the diet was the same. Except in the thyroidectomy group there was no operation. In the pregnancy experiment a diet that contained 16 per cent of casein with corn starch, lard, vitamin, and mineral supplements was used. In other experiments this dietetic change had led to no appreciable deviation from the organ weights found on the usual diet.

ables are classified as dietetic (change in protein consumption), anabolic increase (pregnancy), metabolic decrease (thyroidectomy), and metabolic increase (thyroxin administration). Those instances in which the organ weights deviated from the predicted values beyond the ranges of error given in Table II are printed in bold-faced type.

Although we are well aware that the simplicity of these experiments is only apparent and that a great multiplicity of factors, many of them unknown, are in reality involved, and although we have had experience with the possibilities of error in dealing with weight measurements of such a changing mixture of materials as are combined in the body and its organs, nevertheless we advance the opinion that the all important factor that determined the organ weight

TABLE II

Formula	Average prediction error	Range of error
	<i>per cent</i>	<i>per cent</i>
♂ H.W. = 12.6 (B.W.) ^{0.750} + 8.0.....	1.6	+3.0 to -2.6
♀ H.W. = 12.6 (B.W.) ^{0.750} + 1.5.....	0.7	+1.8 to -1.0
♂ K.W. = 30.0 (B.W.) ^{0.717} + 20.6.....	1.7	+4.6 to -3.2
♀ K.W. = 40.4 (B.W.) ^{0.648} + 12.2.....	1.7	+5.1 to -1.6
♂ L.W. = 92.0 (B.W.) ^{0.838} - 96.0.....	3.7	+7.0 to -7.0

H.W., K.W., and L.W. are respectively the weights of the heart, both kidneys, and liver in milligrams, while B.W. is the body weight in grams.

changes given in Table III was the amount of work imposed on these three organs. In support of this hypothesis the following considerations are advanced.

The work of the heart has been calculated from the rate of volume flow of blood and the mean arterial pressure in heart-lung preparations. Although we have no such measurements in our experiments we know in general that any factor that changes the rate of volume flow of blood will change the amount of work done by the heart so that in deciding whether any of our experimental variables increase or decrease heart work we may use what is generally accepted with respect to the effect of these variables on the rate of blood flow. Now it is shown in Table III, that, in contradistinction to the pro-

nounced effects on the kidneys and liver, changes in protein consumption leave the heart weight unchanged, although the decreased metabolism of protein starvation and the increased metabolism due to the specific dynamic effect of protein should have been accompanied by

TABLE III

Experimental variable	Conditions	Number of rats	Age	Sex	Body weight	Observed weights				Relation to predicted weight			
						Heart	Kidneys	Liver	Protein of liver	Heart	Kidneys	Liver	Protein of liver
						mg.	mg.	mg.	mg.	per cent	per cent	per cent	per cent
Diet changes	No protein but otherwise adequate diet for 10 days	90	110	♂	195	676	1199	6874	1220	+1	-10	-8	-16
	No food for 7 days	90	110	♂	186	657	1163	4900	1042	+2	-10	-32	-25
	Casein in large amounts for 7 days	30	110	♂	194	663	1630	7573	1632	±0	+23	+1	+16
	Liver proteins in large amounts for 7 days	30	110	♂	222	725	1715	11495	2306	-1	+17	+37	+42
Anabolic increase	Pregnancy. Observed 2 days before term	20	100	♀	232	623	1114	8835	1602	-17	-20	+1	+5
Metabolic decrease	Thyroidectomy. Observed 31 days after operation	41	140	♂	192	554	1040	6280	1251	-16	-21	-16	-12
Metabolic increase	Thyroxin administered for 9 days	30	110	♂	210	1010	1845	8376	1728	+44	+30	+5	+15

corresponding changes in the volume flow of blood from the heart which, under the terms of our hypothesis, should have altered its weight. But it must be remembered that the metabolic effects of protein have been determined under basal conditions that did not exist in our experiments. Dock and Lewis (4) have shown that in rats heat production is determined mainly by heat loss and that factors which at an environmental temperature of 28°C. and under basal conditions have pronounced metabolic effects, at a temperature

of 20°C. and under ordinary conditions have their effects largely nullified by compensating changes in the heat production of the voluntary muscles. This damping of the degree of metabolic effect under our special conditions must also be taken into account in interpreting the effect of thyroidectomy and thyroxin administration. Thus it is known that thyroidectomy induces a decrease of about 40 per cent in basal metabolism and so presumably in rate of blood flow, and yet in our experiment there is a decrease of only 16 per cent in heart weight. The conditions in our experiments are so complex that we cannot expect any quantitative parallelism between our heart weights and metabolic measurements made under other and simpler conditions, and we must be content with observing the direction rather than the degree of change. Certainly in the dietetic experiments there was an obvious difference in the activity of the groups deprived of protein and of those given a large surplus of protein, for the former were constantly searching for the food they needed while the latter were quiet and replete, and this difference is one that would diminish the metabolic effects of the variation in protein consumption. But, in addition to this factor, there is another and more general consideration to be taken into account. In the experiments in which no protein was given, the animals, at the time they were killed, had less fat than the controls. Since the heart of the rat has little fat and the body contains a good deal, there was a proportionally greater loss of weight of fat from the body than the heart, so that $H.W./B.W.^{0.750}$ which in essence is our predicted heart weight, would under these conditions be increased. It is this circumstance, more than any other, that may lead to error when we try to compare experimental and control observations on rats of different body weights and different degrees of fatness by the device of expressing the two sets of organ weights in terms of weight per unit of body weight, body surface, or, as here, in terms of some empirically determined power of the body weight. Such quantitative comparisons are valid only if the proportion of fat and water in the bodies of the two groups are alike. Yet for such qualitative purposes as concern us here, where we are considering the significance of gross increases or decreases of organ weight, this quantitative uncertainty need not debar us from drawing

definite conclusions. Thus, for instance, the 10 per cent decrease in kidney weight in fasted rats is not to be put aside as meaningless, for we know that the loss of body fat is a factor that, in itself, will induce an increase and not a decrease in the relation between the actual and predicted weights.

The remaining heart weight change shown in Table III, the 17 per cent decrease of heart weight in pregnancy, is a particular example of the general fallacy involved when formulas from animals under one set of conditions are used to compare organ weights from animals in which other conditions have induced a change in the proportions of the components which make up the body weight. The average body weight of these pregnant rats was 232 gm. and under our standard conditions the heart predicted by the formula is 749 mg. or 17 per cent more than the 623 mg. of heart actually found. But 27 gm. of this 232 gm. of total body weight consisted of embryos which had hearts doing the physical work of circulating blood throughout their bodies. If on this account, neglecting the work of supplying oxygen to the embryos, we subtract their body weight, we leave a net maternal body weight of 205 gm. This gives a predicted heart weight of 682 mg. which is still 8 per cent more than the actual. But it happens that in this case we have protein determinations on the heart and bodies of the pregnant and of a special control group of non-pregnant rats, and though there is not much difference in the concentration of protein in the hearts, we find that the 205 gm. of maternal body has only 14.26 per cent of protein while the controls had 15.86 per cent. The protein in the bodies of the pregnant rats was thus diluted with over 9 per cent of some material not present in the controls. There was no obvious difference in fat content and in this case the added material was water, a substance that takes no oxygen from the blood and that, apart from the additional energy required to move a heavier body weight, leads to no increase in cardiac output. When this weight of water is subtracted from the body weight or when the comparison is made on the basis of the protein content of the heart and body there is no longer any difference between the control and pregnant rats.

The work of the kidney is osmotic work and is the energy used in concentrating the glomerular filtrate. It varies directly as the sum of

the rates of excretion of each urinary constituent multiplied by the \log_n of the ratio between the concentration of each urinary constituent in the urine and plasma (5). In measurements of work done we have found that under conditions similar to those we employed the work of the kidney rises in fairly close correspondence with increase in total nitrogen excretion so that in considering which experiments involve change of work for the kidney we may in general be guided by what is known with respect to their effect on the rate of nitrogen excretion. The decrease in kidney weight when no protein is eaten and the increase when more than the usual amount is consumed follow the known changes in nitrogen excretion. Similarly the decrease in kidney weight after removal of the thyroid gland and the increase when thyroxin is given are in the direction of the changes in nitrogen excretion that occur as a result of changes in protein catabolism and in protein consumption. The 20 per cent decrease in kidney weight in pregnancy is, of course, in part determined by the increased water content of the body. In this case the weight of the embryos must be included since their kidneys were not working and the products of embryonic catabolism were excreted by the maternal kidneys. The protein concentration in the whole 232 gm. of body weight in the pregnant rats was 13.5 per cent as compared with 15.9 per cent in the whole body of the controls. If we assume that all of this dilution was due to water and subtract its weight we have a corrected body weight of 197 gm. and from this a predicted kidney weight of 1250 mg. The actual kidney weight is 1114 mg. and there is still an 11 per cent decrease. This, we believe, is due to a diminution in work on account of the greater utilization of the relatively small amount of protein in the food for the rapid synthesis of protein in the uterus and its contents. This view is supported by the fact that when pregnant rats are given a diet that contains 43 per cent instead of 16 per cent of protein there is an increase instead of a decrease in kidney weight.

In the end the questions we have raised will be answered when experiments can be devised in which the relation between the effective mass of the heart and kidney and the work done by these organs can be measured. In the meantime the considerations we have ad-

vanced are presented, not for their own sake, but as a basis for a study of change in the size of the liver, a field in which there is a need for a preliminary working hypothesis. For while we have a clear idea as to what constitutes the principal work of the heart and kidneys we have no analogous conception with respect to the liver. It may be that the liver has so many functions that no one experimental variable changing only one sort of work will appreciably alter liver size. But we can at least measure the size of the liver under these same conditions and note any agreement or discrepancy between the behavior of liver and heart and kidneys.

There is one difficulty that must be faced before we can approach this problem and that is the circumstance that under certain conditions a not inconsiderable part of the total liver weight consists of fat and glycogen, relatively passive stores of food reserves. We need the actual working machinery stripped of all its fuel and accessories. We believe that the best approach to this is the determination of the total protein content of the liver (6). Part of this liver protein it is true may be a storage protein that comes and goes in accordance with the supply and demand of protein for metabolism. There is, however, accumulating evidence that this labile liver protein is no specialized, inert, and localized deposit analogous to glycogen (7) but that when it exists it is present as a more or less uniform increase in all the principal protein components of the organ (8).

In Table III we have given both the total liver weight and the weight of liver protein, but only the protein changes are considered since we believe that they alone have any precise meaning with respect to the relation between the work and the functioning structure of the liver. The protein deviations represent the changes from the protein content of the liver of a group of 90 rats kept under the same conditions as those observed in the control animals from which the formulas were derived.

The average protein content of the livers of this control group of 90 rats was 1713 mg. The average body weight was 237 gm. It was assumed that if a curve of liver protein for the whole range of body weights had been measured under the same dietary and other conditions it would have paralleled the line in Fig. 1 for total liver weight and would thus have had the same slope, varying as

the 0.838th power of the body weight. On this assumption the liver protein content of control groups of rats of the same body weight as the experimental groups was calculated by multiplying 1713 mg. by $\frac{(\text{experimental body weight})^{0.838}}{(\text{control body weight})^{0.838}}$

Thus in the first experiment in Table III, the control liver protein content at the experimental body weight of 195 gm. is 1713 mg. $\times \frac{195^{0.838}}{237^{0.838}} = 1456$ mg.

In general it will be noted that in the dietetic experiments the direction of change in liver protein is in agreement with kidney weight changes (though there is one remarkable quantitative peculiarity to which we shall return), that in the pregnancy experiment the sign of the deviation is the opposite of that for the heart and kidney, and that in the metabolic experiments all three organs alter in agreement with one another. It is, however, only in the case of the change in liver protein with change in protein consumption that we can go beyond analogy and comparison. The observation made by Dock (9) that it is the liver that uses the greater part of the additional oxygen consumed as a result of the specific dynamic effect of protein is direct evidence in support of the view that work is being done by the liver during the period when amino acids are being absorbed from the portal blood stream.

In the metabolic experiments the results are unambiguous only for the heart because it is the only organ that is not appreciably influenced by changes in food consumption. The removal of the thyroid gland is followed by a decline in the amount of food eaten and the administration of thyroxin leads to an increase of food intake, and so the effect on liver protein might be a secondary result of these associated food changes. We felt it was necessary to clear up this uncertainty with respect to the kidney and liver by repeating these experiments on groups that had fasted for 7 days, and in the case of the liver these experiments should be the more decisive because after a 7 day fast it is to be anticipated that all stores of protein in the liver will have been utilized. But under these new conditions the formulas we have given are no longer applicable. We therefore carried through special control observations, using the same number of rats and contriving the selection in such a way as to get at the end of the 7 days fasting average body weights identical with those of the

experimental groups. However, in the group given thyroxin the loss of body weight was so pronounced that it was not possible to get a comparable control group of the same body weight and in this case it was necessary to calculate the control values from the data given in Table III for 7 day fasted rats.

The body weight of the fasted controls was 186, while the body weight of the fasted thyroxin group was 158 gm. The assumption was made that if continuous curves of organ weight for fasted rats had been obtained against body weight they

TABLE IV
The Effect of Variation in Metabolic Rate after a 7 Day Fast

Experi- mental variable	Conditions	Number of rats	Age	Sex	Body weight	Observed weights				Deviation from fasted controls of same body weight			
						Heart	Kidneys	Liver	Protein of liver	Heart	Kidneys	Liver	Protein of liver
						mg.	mg.	mg.	mg.	per cent	per cent	per cent	per cent
Metabolic decrease	Thyroidectomy. Ob- served 29 days after operation	25	110 days	♂	173 gm.	532	969	4462	954	-15	-15	-2	-2
Metabolic increase	Thyroxin administered for 9 days	20	110	♂	158	827	1342	4995	1058	+40	+30	+17	+16
	Dinitrophenol adminis- tered for 7 days	30	110	♂	183	641	1188	4676	1018	±0	-3	-7	-6

would have paralleled the lines in Fig. 1 and would have had the same slopes. On this assumption the control heart for the thyroxin group is $657 \times \frac{158^{0.75}}{186^{0.75}} = 592$, the control kidneys $1163 \times \frac{158^{0.717}}{186^{0.717}} = 1034$, the control liver $4900 \times \frac{158^{0.838}}{186^{0.838}} = 4280$ and the control liver protein $1042 \times \frac{158^{0.838}}{186^{0.838}} = 910$.

The results given in Table IV indicate that under these conditions thyroidectomy leads to no significant decrease in liver protein relatively to fasted controls. On the other hand, thyroxin, even in fasted rats, leads to a 16 per cent increase in liver protein. The heart

changes are almost the same as those in fed rats and in the kidney only the thyroidectomy decrease is lessened.

This demonstration of the pronounced effect in both fed and fasted animals on heart, kidneys, and liver protein of an increase in metabolic rate induced by thyroxin, raises the question as to whether all of the organ weight changes we have found may be due to alterations in the rate of metabolism of the organs themselves. Under this view, for instance, the alteration of kidney and liver protein with change in protein intake would be ascribed not to the need of more oxygen for work alone but to the fact that in these organs, the metabolic rate of the whole kidney and liver, not only of its directly working parts, varied with protein intake. This hypothesis can be tested by observing the effect of dinitrophenol which markedly increases organ metabolism without increasing the work of the heart, since the additional oxygen required is obtained not by increased output of blood by the heart but by taking more than the usual proportion of oxygen from the blood in the capillaries and without increasing the work of the kidneys since under its influence there need be no increase in protein catabolism. The results as shown in Table IV show no increase in heart, kidney, or liver protein after dinitrophenol in spite of the fact that in the doses used there was a pronounced increase in organ metabolism (10). We conclude therefore that the mechanism responsible for change in organ size is not the total metabolic rate within the organ, and revert to the hypothesis that it is work that determines organ size though it may well be that the special oxygen requirements entailed by work are an essential part of the mechanism by which the equilibrium between work and organ size is maintained.

The general agreement between the direction and extent of the kidney and liver changes suggest that whatever increases the work of the kidney generally increases also the work of the liver. But there are two rather marked discrepancies in Table III.

In the pregnancy experiment the heart and kidneys became much smaller relatively to the body weight but this is not true of the liver protein. Instead of a decrease a 5 per cent increase was found. This is the more remarkable because the two considerations which led us to believe that the decrease in heart weight was only apparent (the addition of water to the mother's body and the work of the fetal

hearts), both apply in the case of the liver. If similar corrections of maternal body weight are applied here we find that the liver is not 5 per cent but 21 per cent greater than the controls. This result suggests that in pregnancy the liver may have some special work to do that leads to its enlargement.

The other disagreement does not involve any change of direction and is only quantitative, but the 42 per cent increase in liver protein when large amounts of dried liver are taken as food is of a different order of magnitude in relation to the other liver changes. A similar experiment with dried whole kidney as food gave almost as great an increase and so we can conclude that this result is not due to any substance peculiar to liver tissue. Since an equally large consumption of casein, which contains no nucleic acid, led only to a 16 per cent increase in liver protein, the first possibility to explore would be that the metabolism of nucleic acid imposes a special load of work on the liver. Experiments to decide this point are now under way.

In conclusion it is well to remember that what we have called in this paper experimental variables are not changes of only one factor at a time within a system in which all the important variables are known and measured. Even when the only variation consisted in giving more or less protein as food, or in adding or subtracting thyroxin, much more was effected than an alteration of protein supply or rate of metabolism. The weights of the heart, kidneys, and liver protein were doubtless influenced by a multiplicity of factors other than those we have singled out and among them may be many whose operation we do not even suspect. So our opinion that the observed facts are at present best accounted for by the supposition that the main factor that determines the weight of the heart, kidneys, and liver protein is the amount of work these organs are required to perform is only a working hypothesis. It is presented because it may be useful in planning further experiments with other and more precise methods for the analysis of the mechanism of change in the amount of functioning liver tissue and in the investigation as to what constitutes its principal work.

We are indebted to Mr. W. Lew for most of the work in the care and management of the animals and to Mr. D. Karnofsky for the operations on the thyroidectomized groups.

CONCLUSIONS

1. The ratios between the rates of growth of the body and of the heart, kidneys, and liver are approximately uniform between 40 gm. body weight and the body weight at maturity in the albino rat. The male and female hearts grow at 0.75 times the rate of growth of the body, the male kidneys at 0.717 times, the female kidneys at 0.648 times, and the liver at 0.838 times the rate of growth of the body as a whole.

2. Formulas for the prediction of organ weight from body weight were derived from the data on 1591 albino rats kept under constant conditions.

3. A series of experiments in which dietetic and metabolic variables were introduced into otherwise constant conditions showed that the heart weight was not affected by diet, and that both kidney weight and weight of liver protein (used as a measure of effective liver size) varied in the direction of change in the protein content of the diet. Decrease in rate of metabolism induced by thyroidectomy and increase in metabolism following the administration of thyroxin led to a corresponding fall and rise of heart, kidney, and liver protein weight. These results were confirmed in experiments on fasted rats with the exception that under these conditions thyroidectomy did not appreciably decrease liver protein weight relatively to fasted controls. Increase in organ metabolism due to dinitrophenol had no effect on organ weight.

4. When experimental changes alter the composition of the body with respect to fat or water, the comparison of experimental and control organ weights in terms of any one function of body weight is fallacious.

5. Conditions that change kidney weight usually change liver protein weight in the same direction and roughly to the same degree. The possible meaning of two exceptions to this rule is discussed.

6. The observations made are regarded as supporting the hypothesis that, after weaning, change in the weight of the heart, kidney, and liver protein is determined mainly by change in the amount of work done by these organs.

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