

CLINICAL CALORIMETRY

TWENTY-FIRST PAPER

THE BASAL METABOLISM OF DWARFS AND LEGLESS MEN WITH OBSERVATIONS ON THE SPECIFIC DYNAMIC ACTION OF PROTEIN*

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In order to establish more fully the law that the total body metabolism is proportional to the surface area, it is important to establish the law not only for people of normal size and shape, but also for those who are deformed. If the body surface be a true index of the metabolism, and if the body surface be accurately measured, then dwarfs or men with their legs cut off would show proportionally the same basal metabolism per square meter of surface as do normally shaped individuals. But if this relationship holds, is the increase in heat production which follows the ingestion of large quantities of meat the same as in persons of normal shape? It was to try to answer these questions that this series of dwarfs and legless men were studied in the Sage calorimeter at Bellevue Hospital.

THE BASAL METABOLISM OF MEN OF UNUSUAL SHAPE

History.—The basal metabolism of normal individuals has been well established by the large number of normal controls gathered by Benedict, Emmes, Roth and Smith;¹ by Means² and by Gephart and Du Bois.³ The total metabolism of dwarfs has been investigated in one case each by Rubner⁴ and by McCrudden and Lusk.⁵

Rubner studied a very small dwarf who was 20 years old and

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1. Benedict, F. G., Emmes, L. E., Roth, P., and Smith, H. M.: The Basal Gaseous Metabolism of Normal Men and Women, *Jour. Biol. Chem.*, 1914, **18**, 139.

2. Means, J. H.: Basal Metabolism and Body Surface, *Jour. Biol. Chem.*, 1915, **21**, 263.

3. Gephart, F. C., and Du Bois, E. F.: The Determinations of the Basal Metabolism of Normal Men and the Effect of Food, *THE ARCHIVES INT. MED.*, 1915, **15**, Part 2, p. 835.

4. Rubner, M.: *Biologische Gesetze*, Marburg, 1887, p. 10; *Beiträge zur Ernährung im Knabenalter*, Berlin, 1902, p. 45.

5. McCrudden and Lusk: The Metabolism of a Dwarf, *Jour. Biol. Chem.*, 1912-1913, **13**, 447.

weighed but 6.6 kg., and who "behaved like a fully grown man." His observations were not made under conditions of complete rest, and so are not comparable to our findings. Rubner, however, calculated that the metabolism per square meter, using Meeh's formula, was but slightly higher than that of a breast-fed infant of similar weight. "The larger metabolism of the dwarf," he writes, "is explained by his greater activity, while the infant is very quiet . . . and neither stands nor walks." This showed, according to Rubner, that metabolism was dependent on surface area, not on age.

McCrudden and Lusk's case was in a boy of 17 years, 113 cm. tall and weighing 21.3 kg. By the height-weight chart his surface area is, therefore, 0.8 square meters. He was a patient described by C. A. Herter⁶ under the diagnosis of intestinal infantilism. This is a condition in which the arrest of growth is associated with a group of symptoms based on chronic intestinal intoxication. It is associated with fair mental development, marked abdominal distention, moderate anemia, but most strikingly by frequent periods of diarrhea with fatty and putrefying stools. No definite history of this patient is given, but it is one of the cases used by Herter in the description of the syndrome. Practically normal urinary findings on the same case are reported by McCrudden.⁷ The patient was studied in a small calorimeter in Dr. Lusk's laboratory, and the routine was practically the same as is now followed in the Sage calorimeter. The results are, therefore, directly comparable to those reported in this paper. Five observations were made on the dwarf, but only one was a true basal experiment, while on the other occasions he had small amounts of food before entering the calorimeter. The one basal observation has been summarized in Table 1, and shows a normal metabolism per square meter of surface area.

In this series we wish to report the metabolism of five dwarfs; two of the achondroplastic type, one rachitic and two with involvement of the glands of internal secretion. Added to this group are two men who had lost both legs. The basal observations in the calorimeter were made in the routine way followed in this laboratory, and fully described in the third and fourth papers of this series.⁸ The subjects had had no food for at least fifteen hours, and during the observation remained quietly lying on a bed.

6. Herter, C. A.: On Infantilism from Chronic Intestinal Infection, 1908.

7. McCrudden: Chemical Studies on Intestinal Infantilism, *Jour. Exper. Med.*, 1912, **15**, 107. McCrudden and Fales: *Ibid.*, 1912, **15**, 113.

8. Gephart, F. C., and Du Bois, E. F.: The Organization of a Small Metabolism Ward, *THE ARCHIVES INT. MED.*, 1915, **15**, 829. Determination of the Basal Metabolism of Normal Men and the Effect of Food, *ibid.*, p. 834.

We have followed Rischbieth's⁹ classification of dwarfs, so careful description of types will not be discussed here. The differentiation of the rachitic, the achondroplastic and the ateliotic (the perfectly proportioned) types is not difficult with the help of the Roentgen ray. However, we have been puzzled in the distinction between the myxedematous and true dwarfism (or ateliotic) types. The skeleton of the ateliotic dwarfs has the same characteristics of bone formation as has the mild cretin, for the cartilage disks of the long bones (according to Rischbieth, and Sternberg¹⁰) persist throughout life, and the square shaped skull and cretinoid facial appearance may also be present. Both have defective sexual development and both may be mentally defective. Brissaud¹¹ classifies myxedema, ateliosis and infantilism in one group and Sternberg admits that this is a possible classification. This difficulty in diagnosis confronted us several times in choosing suitable subjects for the investigation.

CASE HISTORIES

CASE 1.—Raphael De P. (Figs. 1 and 2), achondroplastic dwarf, born in Italy, aged 35; a kitchen helper; height 134.7 cm.; weight 40.9 kg.

History.—The family history is negative; no other dwarf in the family for three generations. Had severe illness when a few months old. Since then always well except for chancroid infection twelve years prior to the test. Has been married for eight years to a woman of normal size; has two children, both of normal size.

Physical Examination.—An active, cheerful Italian of normal mentality. The physical examination is negative save for the extremities. All the long bones seem shortened, with slight outward bowing and proportionally large epiphyses. The thighs and upper arms are particularly short. The muscles are powerful. Hands are flat and short, fingers are fat and stubby. Urine, negative. Blood pressure: systolic 120 mm.; diastolic, 90 mm.

CASE 2.—George F.,* hypopituitarism; myxedema; born in Ireland, aged 48; single; a clerk; height 148.8 cm.; weight 53.1 kg.

History.—The family history is negative. He has always been small in stature, though active. For six years he has had occasional attacks of edema, particularly about the eyes, feet and hands. For three years he has had slight shortness of breath and failing vision. He sleeps a great deal and perspires very little. He has had no sexual power for many years.

Physical Examination.—A short, rather fat individual with cretinoid face and feminine type of body. The genitalia are small, the breasts are large. There is no hair except on the head and eyebrows, and this is dry and slightly coarse.

9. Rischbieth, H., and Barrington, A.: *Dwarfism*, Treasury of Human Inheritance, London, 1912, Part VII, Sec. xv A.

10. Sternberg, M.: *Vegetationsstörungen und Systemerkrankungen der Knochen*, Wien., 1899; *Nothnagel's specielle Pathologie und Therapie*, Vienna, 1903, 7, Part 2.

11. Brissaud, E.: *De l'infantilisme myxedemateux*, Nuov. iconog. de la Salpêtrière, 1897, 10, 240-282.

*This patient was carefully studied by Dr. W. M. Krause, who reported the case in the *Jour. Nerv. and Ment. Dis.*, 1917, 45, 193.

The arms are long, the hands of trident type. There was general edema without much pitting on admission, but after a week in the hospital this disappeared, leaving a yellowish, dry, much wrinkled skin. Mentally, he is like a well-behaved child and is always good-natured.

Laboratory Findings.—Blood, normal. Urine occasionally showed small amounts of albumin and rare granular casts; 4,000 c.c. of water intake daily for ten days caused no increase in weight. Phenolsulphonephthalein test, 55 and 63 per cent. in two hours. Wassermann negative. Glucose sugar tolerance,

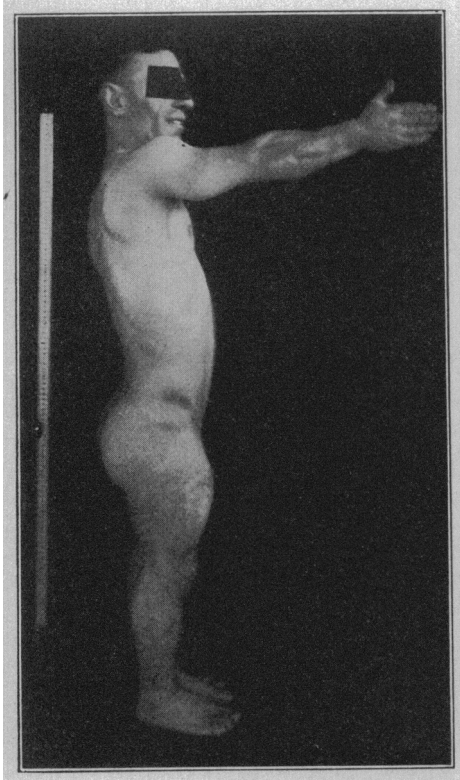


Figure 1

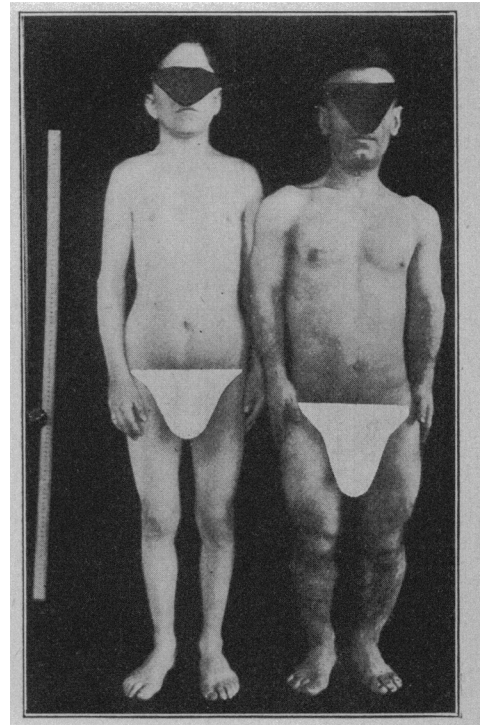


Figure 2

Fig. 1.—Raphael deP. Achondrodystrophy. The meter stick is opposite the spine.

Fig. 2.—Raphael deP. and a dwarf of ateliotic type.

more than 400 gm. Roentgenogram of hands showed epiphyseal ends of bones to be atrophic. The epiphyseal lines are still visible, particularly the lower ends of the radius and ulna. The head shows a markedly enlarged and somewhat eroded sella turcica.

CASE 3.—Samuel G., achondroplastic dwarf, born in Germany, aged 29; single; an actor; height 123.5 cm.; weight 34.9 kg.

History.—The family history is negative. His arms and legs have always been very short for his age. Except for an occasional attack of nausea and vomiting, he is perfectly well. Mentally, he is slow and defective; sexually, he is well developed.

Physical Examination.—Negative, save for the extremities. The torso is of normal shape and size; the arms and legs very short. The head is large and square, with a high forehead and a saddle-shaped nose. The hard palate is high. The extremities are very short, particularly the upper arms and legs, but the muscular development is good. The feet and hands are almost normal size and large for the rest of the extremities. The genitalia are of mature development, the body hair is abundant and of normal masculine distribution. The urine is normal.

CASE 4.—Patrick W. (Figs. 3, 4, 5 and 6), rachitic dwarf, born in United States, aged 38; actor; height 123.8 cm.; weight 37.3 kg.

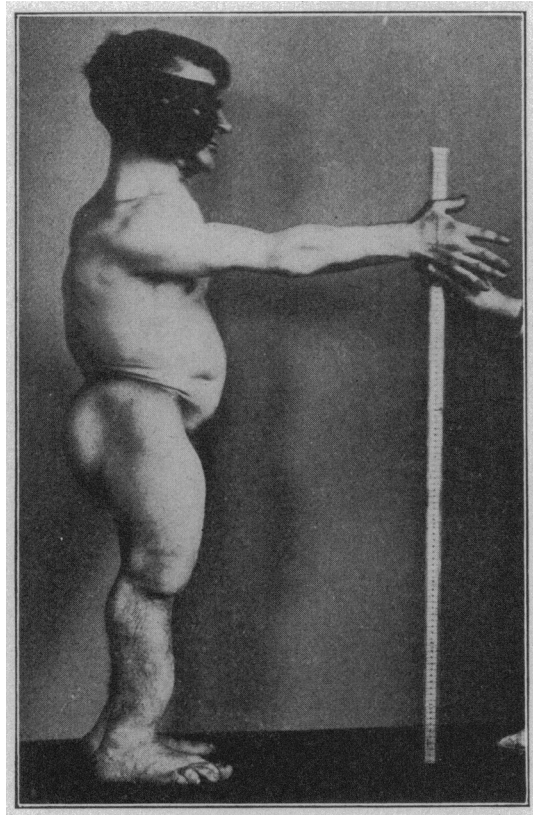


Fig. 3.—Pat W., rachitic dwarf.

Patient says he was normal until 3 years old when he became moody and his body became distorted. He had walked and talked at the usual age. He has had gonorrhea three times; twelve years prior to the test he had syphilis, followed by very severe nephritis. During this attack he was very edematous and the abdomen was tapped eight times. Since then he has felt perfectly well.

Physical Examination.—A small, misshapen dwarf with marked curvature of the spine and the longer bones. The head appears normal. The chest is very narrow in the upper portion, with a prominent sternum. There is marked flaring of the lower ribs, with Huntington's groove and marked rosary. The spine shows left lateral curvature in the lower thoracic region, with a slight kyphosis. The legs are very short and markedly bent. The feet appear normal.

The arms are short, but the bones are only slightly curved. The epiphyses of all the long bones are large. The genitalia are well developed; the body hair is of masculine type of distribution.

Laboratory Findings.—Urine was negative; specific gravity, 1.025; albumin, negative. Microscopic examination, negative.

CASE 5.—Irwin E., myxedematous dwarf, born in United States, aged 32; actor; height 134 cm.; weight 37.4 kg.

History.—He has always been of small size. At 10 years of age he was short and weighed but 40 pounds. His school work was not very good, as he failed four times in grammar school. He passed for high school when he was

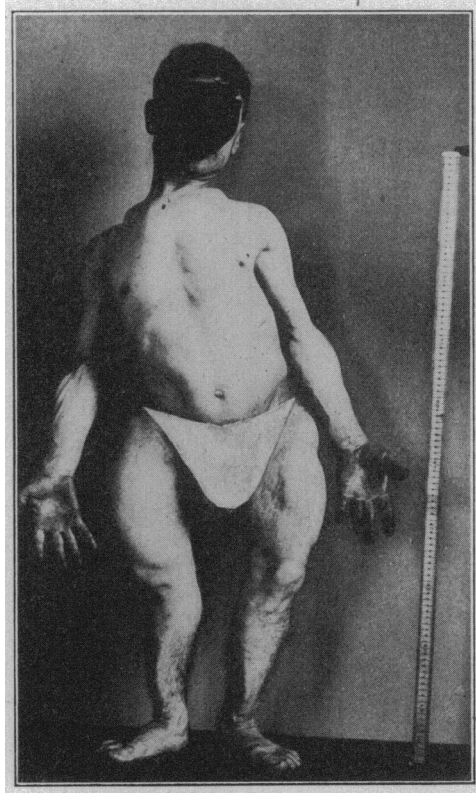


Fig. 4.—Pat W.

15 years old, and stayed there only one year. He is sexually mature, but inactive. The hair on his head has always been soft and plentiful. He perspires freely.

Physical Examination.—He appears like a well developed boy of 14 years. The facies suggests cretinism—thick eyebrows, puffy eyelids, broad nose, wide maxillae, broad jaw and large, widely spaced teeth. There is a pad of fat between the shoulders and a slight degree of adiposity. The hands are short and stubby; the skin slightly dry, but soft and smooth. The genitalia appear normally developed, but the secondary characteristics are scant for there is no hair on the face, in the axillae or on the body, and the pubic hair is of the feminine configuration. The voice is that of male puberty. Otherwise the

physical examination is not remarkable. Blood pressure: systolic, 95 mm.; diastolic 65 mm.

Roentgenogram of head shows a slightly enlarged sella turcica. In the hand there is some hypo-atrophy of the terminal tufts of the phalanges. The epiphyses of the radius and ulna are not united. The epiphyseal lines of the phalanges are clear.

CASE 6.—Harry J. (Fig. 7, described in Paper 9), a legless man, born in the United States, colored, aged 34; beggar. Length is approximately 103 cm., weight 54.6 kg.

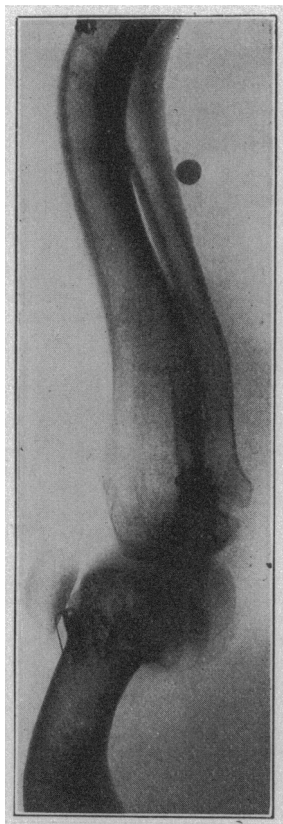


Fig. 5.—Pat W. Roentgenogram of knee.

History.—Both legs were cut off by a train when the patient was 6 years old, and since then he has propelled himself on wheels. Seven years prior to the test the right side of the body suddenly became numb and the right arm was completely paralyzed. Slight power returned slowly. He had urethritis seven years previous to the examination, possibly with a chancre, though no secondary manifestations developed.

Physical Examination.—Very muscular negro with short leg stumps. *Face:* Forehead is normal but right side of face is paralyzed; mouth droops and tongue deviates slightly to right. *Chest* is unusually broad and deep, with very powerful muscles in the back, neck and left shoulder and arm. The waist is very narrow; the hips narrow, with poorly developed muscles. The right arm is paralyzed and the muscles are of moderate size but flabby. The

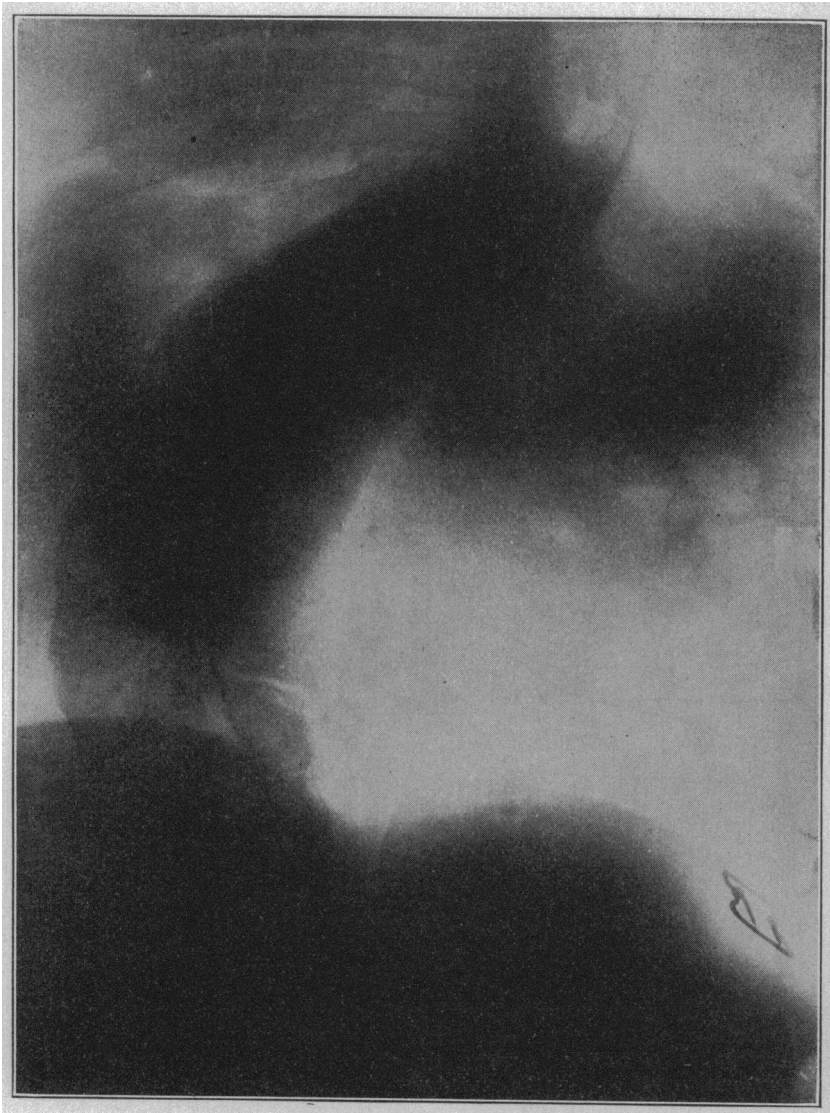


Fig. 6.—Pat W. Spine.

reflexes are exaggerated. The right leg is a very short stump with flabby muscles. The left leg is amputated just above the knee and the stump tapers sharply from the perineal level. The muscles are small and weak. Blood pressure: systolic, 188 mm.; diastolic, 130 mm.

Urine, negative. Wassermann, negative.

CASE 7.—Robert L. (described in Paper 9), a legless man, born in the United States, aged 43; beggar; length about 125 cm.; weight 63.8 kg.

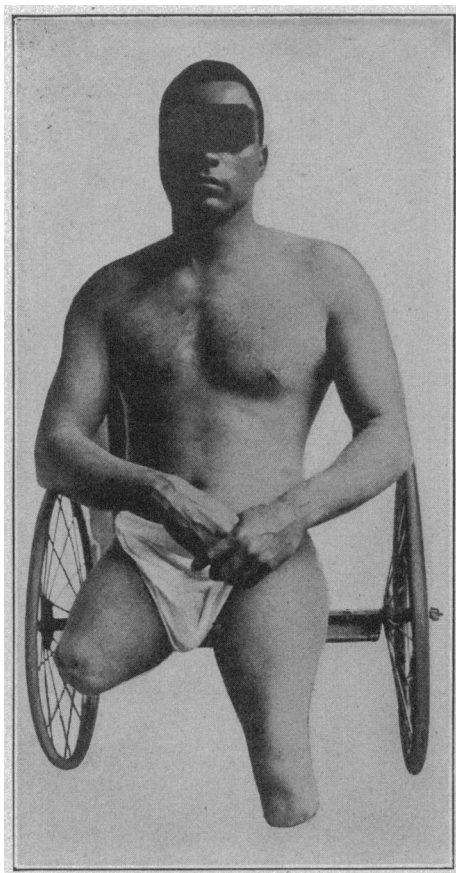


Fig. 7.—Harry J.

History.—The patient was a boiler maker for over twenty years and was always healthy and strong. He had syphilis and urethritis nineteen years ago, for which he received treatment for five months. Five years prior to the examination he was hit by a railroad train and both his legs had to be amputated. He now feels well and supports himself by selling pencils. He walks about a mile every day, with crutches.

Physical Examination.—A heavily built, healthy looking man with fat cheeks and prominent abdomen. His chest is large; his arms muscular. The left thigh is cut off just below the level of the perineum. The right leg is cut off just below the level of the knee and the thigh muscles are firm and strong. Otherwise, the patient appears normal, except that over the left lung there are heard many dry, crackling râles, though resonance, tactile fremitus, vocal fremitus and breath sounds are normal.

TABLE 1.—SUMMARY

Case Number and Name	Subject	Age	Height, Cm.	Weight, Kg.	Surface Area, Sq. M. Linear Formula	Calories per Sq. M. per Hour	Variations from Average Normal 39.7 %	Average R. Q.	Total Calories Measured		Divergence of Direct from Indirect, Per Cent.	Average Calories per Hour, Indirect
									Indirect	Direct		
6. Harry J. *	Legless man	35	103±	54.61	1.34	41.3	+4.0	0.80	110.67	106.42	-3.9	55.34
7. Robert L.	Legless man	43	125±	63.81	1.43	41.3	+4.0	0.80	176.90	178.22	+0.7	58.97
4. Patrick W.	Rachitic dwarf	38	123.8	37.31	1.20	41.0 •	+3.0	0.81	98.27	97.74	-0.5	49.17
1. Raphael DeP.	Achondroplasia	35	134.7	40.86	1.24	42.2	+6.3	0.81	104.66	102.20	-2.3	52.33
3. Samuel G.†....	Achondroplasia	29	123.5	34.92	1.03	(46.9)	(+23.0)	(0.82)	(39.58)	(38.26)	-3.3	52.76
5. Irwin E.	Myxedema	32	134.0	37.37	1.17	29.5	-25.7	0.85	63.98	70.31	+1.9	34.49
2. George F.	Hypopituitary Hypothyroid	48	148.9	53.05	1.51	81.1	-22.0	0.83	96.57	94.51	-2.1	48.28
J P.‡.....	{ "Intestinal Infantilism"	17	113.3	21.3	0.8	38.2	-4.0	0.79	61.12			

* Quiet experiment, 5/6/16.

† Forty-five-minute period only.

‡ McCrudden and Lusk's case.

Nauseated. Other observations two hours.

DISCUSSION OF RESULTS

Two of the experiments here recorded were technically unsatisfactory and cannot be considered as giving accurate evidence as to the level of the basal metabolism. The achondroplastic dwarf, Samuel G., was nauseated in the calorimeter and the high figures obtained in his brief observation might have been due to the same factor which caused his vomiting. The legless negro, Harry J., was also restless the first time he was in the calorimeter. While he did not move often, his deformity and paralysis of the right arm made each movement a great exertion. In his second experiment he was quiet and the results were satisfactory.

This leaves good determinations of the basal metabolism of seven men of unusual body shape. Five give figures within the normal limits when the results are calculated according to the surface area. These individuals are the two legless men, Harry J. and Robert L., the rachitic dwarf, Patrick W., the achondroplastic dwarf, Raphael de P., and the dwarf, J. P., with intestinal infantilism, described by McCrudden and Lusk. Two dwarfs give results distinctly below the normal. These are Irwin E. and George F., both of whom had many of the characteristics of cretinism, a condition which is always accompanied by a diminution in the heat production.

It therefore seems true that people with abnormal body shape, but with normal glands of internal secretion, have a metabolism which conforms to their surface area. It is therefore possible that the height of metabolism may be a method for differentiating the ateliotic and myxedematous dwarfs.

THE SPECIFIC DYNAMIC ACTION OF PROTEIN

Many investigators have studied the increased heat production which accompanies the metabolism of protein. The literature has been thoroughly reviewed and discussed by Lusk¹² in his book on nutrition, so that only the most important references are given here.

Von Mering and Zuntz¹³ believed that the increased metabolism was due to intestinal work following ingestion of food. This was disproved, however, by the fact that fat and carbohydrate increase metabolism far less than an equal quantity of protein. Rubner¹⁴ and Magnus-Levy¹⁵

12. Lusk, G.: *The Elements of the Science of Nutrition*, Ed. 3, Philadelphia, 1917.

13. Von Mering and Zuntz, N.: In wiefern beeinflusst Nahrungszufuhr die thierischen Oxydationsprocesse, *Pflüger's Arch. f. d. ges. Physiol.*, 1877, **15**, 634.

14. Rubner, Max: *Die Gesetze des Energieverbrauchs bei Ernährung*, Leipzig, 1902.

15. Magnus-Levy, Ad.: Ueber die Grösse des respiratorischen Gaswechsels unter dem Einfluss der Nahrungsaufnahme, *Pflüger's Arch. f. d. ges. Physiol.*, 1894, **55**, 1.

fed bones to a dog and obtained but slight increase in metabolism in spite of the intestinal irritation and activity. Rubner¹⁴ believed that this "specific dynamic action" was due to the cleavages and oxidations necessary to make the foodstuffs available for use by the body cells. The heat given off by these preliminary reactions constituted the waste heat of the dynamic action. In the case of protein, part of the heat, he thought, was derived from the carbohydrate portion burned, but chiefly it arose from the chemical reactions of the remainder of the protein molecule, whose end-products appear in the urine, mostly as urea. This energy, he thought, was liberated unused by the organism. Voit¹⁶ believed that the cells of the body were stimulated to a higher metabolism by food being brought to them. Lusk¹⁷ gave amino-acids and glucose to normal and phlorhizinized dogs. The metabolism of the normal dog was stimulated by both foodstuffs, but the phlorhizinized dog had no change in metabolism when glucose was administered and totally excreted. However, the amino-acids, glycolic and alanin, though unoxidized and excreted with all their energy as sugar and urea, still caused an increase of metabolism. The conclusion is clear that it is not the energy contents of the amino-acids themselves, for those were excreted, but, to quote from the original, "that intermediary products, such as glycolic acid or lactic acid, provide the stimulus. These experiments afford conclusive proof of a true chemical stimulation of protoplasm within the mammalian organism, and offer a logical explanation of the specific dynamic action of protein."

It was to find out where this chemical stimulation occurred, whether in the muscles or in the internal organs, that the following experiments were made at the suggestion of Dr. Lusk. Individuals were taken with normal torsos, but a marked variation in the size of their extremities. If the specific dynamic action of a test protein meal were due to the muscle volume or the surface area, then an achondroplastic dwarf and legless man should show a proportionally smaller stimulation of metabolism than did the normal controls. If the action were due to one of the internal organs, the response of all the subjects tested should be approximately the same.

The subjects chosen were a legless man, an achondroplastic dwarf and three normal controls whose weight closely approximated that of the two abnormal cases. The basal metabolism was determined, following the usual routine technic of this laboratory, fifteen to eighteen hours after the last food. Within the next week the subject was prepared as for a basal observation, but in the morning he was given a

16. Voit, C.: *Physiologie des Stoffwechsels und der Ernährung*, Leipzig, 1881, p. 308.

17. Lusk, G.: *Animal Calorimetry*, XI, An Investigation Into the Causes of the Specific Dynamic Action of the Foodstuffs, *Jour. Biol. Chem.*, 1915, **20**, 555.

large protein meal. This consisted in all cases, except that of Louis M., of about 660 gm. of thoroughly scraped lean beefsteak, chopped very fine and cooked only superficially. In each case a sample was analyzed for protein and fat. A small amount of stewed tomatoes and "Kaffee Hag" were allowed in order to make the food more palatable. Louis M., whose observations are taken from the work of Gephart and Du Bois,¹⁸ had been given the same meal with the addition of 100 gm. of fat. When the subject had finished eating he was put in the calorimeter, and two hours after the start of the meal the observation was begun. In several cases the metabolism was also determined for a thirty-minute period, starting one and one-half hours after the start of the meal. All of the subjects received approximately the same amount of protein (24 gm. of nitrogen) and the temperature of the calorimeter was the same for all observations, so that the results are directly comparable; for Rubner¹⁴ pointed out that a change in temperature has a marked effect on the specific dynamic action of protein, and Gigon¹⁹ claimed that the dynamic action did not vary directly with the amount of protein ingested.

The urine was collected in hourly periods, when this was possible, and each sample was analyzed separately for nitrogen, and in most observations for sulphur. In this way the speed of the nitrogen and sulphur excretion could be compared with the increase in metabolism (Table 2). The urinary nitrogen was determined by the usual Kjeldahl method and the sulphur by Benedict's method. The amount of protein and fat ingested was calculated from analyses of each sample of steak used.

CASE HISTORIES

CASE 8.—S. K., normal control, born in Japan, aged 33; medical student; height 161.5 cm.; weight 49.5 kg.

The history is entirely negative, except that fifteen years prior to examination he had slight symptoms of beriberi, which rapidly disappeared when he changed his diet. He exercises a great deal, mostly at jiu jitsu and wrestling.

The physical examination is negative. He is a Japanese of very marked muscular development and good physique.

CASE 9.—G. T. B., normal control, born in the United States, aged 25; medical student; height 164.5 cm., weight 54.4 kg.

He has always been fairly well, but never athletic or very strong. His life has been a sedentary one, particularly for some months previous to the test, during which he has been studying for examinations.

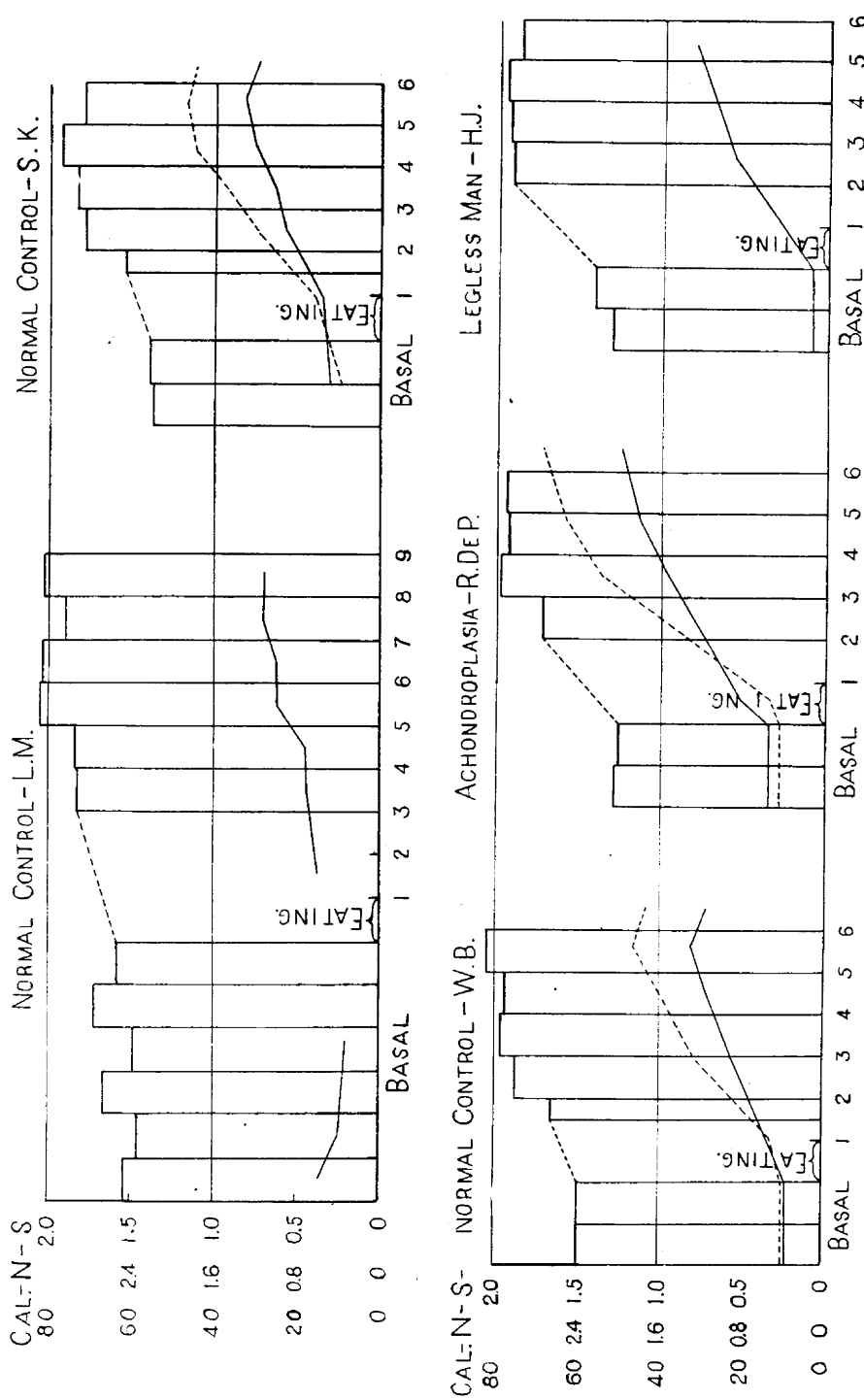
The physical examination is negative.

CASE 10.—Louis M.,¹⁸ normal control, born in Germany, aged 22 years; barber; weight 51.7 kg.

A short, thin, normal individual with small frame and muscles.

18. Gephart, F. C., and Du Bois, E. F.: Determination of the Basal Metabolism of Normal Men and the Effect of Food, *Clinical Calorimetry*, Fourth Paper, *THE ARCHIVES INT. MED.*, 1915, **15**, 835.

19. Gigon, Alfred: Ueber den Einfluss der Nahrungsaufnahme auf den Gaswechsel, *Arch. f. Physiol.*, 1911, **140**, 544.



The observations brought out several points of interest. The graphic chart shows that the metabolism had risen to a considerable degree one and one-half hours after the meal, and nearly to the maximum intensity two hours after eating. It remained at the high level for at least seven hours, with the maximum heat production between the fourth and sixth hours following ingestion of food. This shows that the absorption of food from the intestine is rapid, for certainly within one and one-half hours after partaking of food it has been partly absorbed from the bowel and is being metabolized.

TABLE 2.—NITROGEN AND SULPHUR EXCRETION IN THE DOG (AFTER RUBNER)

Period	Sulphur	Nitrogen	$\frac{N}{S}$
9-3	0.448	5.57	12.4
3-9	0.387	8.94	23.1
9-3	0.257	5.32	20.7
3-9	0.131	2.66	20.3

But what is the index of the true protein metabolism? Voit emphasized the fact that the amount of protein eaten was not good evidence of the amount metabolized, but that the urinary nitrogen was a much more direct index. But even though the urinary nitrogen is direct evidence, its hourly value is still rising for some hours after the stimulation of protoplasm has reached its maximum. This same fact has been observed in the study of dogs by Williams, Riche and Lusk,²⁰ who point out that there is a delay in the excretion of nitrogen following the metabolism of protein. They found that after giving 700 gm. of meat to the dog the maximum increase of metabolism was reached in two hours, but that the urinary nitrogen excretion did not reach its maximum until the sixth hour. There is, during this time, a temporary accumulation of nonprotein nitrogen, largely of the urea portion, in the blood and tissues, as was shown by Folin and Denis²¹ and by Miss Wishart.²² It was also shown by Reilly, Nolan and Lusk²³ that in a dog made diabetic with phlorhizin, the sugar derived from the

20. Williams, Riche and Lusk: Metabolism of the Dog Following the Ingestion of Meat in Large Quantities, *Jour. Biol. Chem.*, 1912, **12**, 349.

21. Folin, Otto, and Denis, W.: Protein Metabolism from the Standpoint of Blood and Tissue Analysis, *Jour. Biol. Chem.*, 1911-1912, **11**, 87.

22. Wishart, Mary: Animal Calorimetry, Paper IX. The Influence of Meat Ingestion on the Amino-Acid Content of Blood and Muscle, *Jour. Biol. Chem.*, 1915, **20**, 535.

23. Reilly, F. H., Nolan, F. W., and Lusk, G.: Phlorhizin Diabetes in Dogs, *Am. Jour. Physiol.*, 1898, **1**, 395.

protein was excreted more rapidly than was the nitrogen. This is direct proof of the delayed excretion of nitrogen after its metabolism. Lusk²⁴ and Csonka²⁵ have shown that the administration of amino-acids to the phlorhizinized dog causes a maximal rise in both the heat production and sugar elimination in the first one or two hours, which indicates

TABLE 3.—NITROGEN-SULPHUR RATIOS AFTER MEAT INGESTION

Name	Date	Time	Nitrogen per Hour, Gm.	Sulphur per Hour, Mg.	N — S	Remarks
R. DeP.	3/15	7:20 a. m. to 1:10 p. m.	0.60	Basal
	3/16	5:00 a. m. to 8:55 a. m.	0.57	31.9	17.7	662 gm. meat at 9:00 a. m.
		8:55 a. m. to 9:55 a. m.	0.87	35.3	24.7	
		9:55 a. m. to 12:17 p. m.	1.27	82.6	15.7	
		12:17 p. m. to 1:32 p. m.	1.61	135.6	11.9	
		1:32 p. m. to 3:04 p. m.	1.88	159.7	11.8	
		3:04 p. m. to 4:02 p. m.	2.02	173.0	11.7	
S. K.	5/16	9:27 a. m. to 1:26 p. m.	0.46	22.7	20.2	Basal
	5/18	9:15 a. m. to 11:23 a. m.	0.55	38.8	14.2	660 gm. meat at 8:20 a. m.
		11:23 a. m. to 12:22 p. m.	0.91	74.8	12.2	
		12:22 p. m. to 1:23 p. m.	1.02	94.1	10.9	
		1:23 p. m. to 2:32 p. m.	1.19	111.8	10.1	
		2:32 p. m. to 3:30 p. m.	1.29	117.9	10.9	
		3:30 p. m. to 4:24 p. m.	1.19	111.7	10.6	
W. B.	5/23	8:45 a. m. to 1:02 p. m.	0.37	25.0	14.6	Basal
	5/25	6:55 a. m. to 8:23 a. m.	0.54	32.7	16.6	600 gm. meat at 8:25 a. m.
		8:23 a. m. to 10:29 a. m.	0.61	34.4	17.7	
		10:29 a. m. to 12:30 p. m.	0.92	80.8	11.4	
		12:30 p. m. to 1:30 p. m.	1.12	104.3	10.7	
		1:30 p. m. to 2:28 p. m.	1.22	118.2	16.3	
		2:28 p. m. to 3:29 p. m.	1.13	110.7	10.2	
Harry J.	5/10	5:00 a. m. to 9:46 a. m.	0.38	25.7	14.7	660 gm. meat at 9:00 a. m.
		9:46 a. m. to 1:48 p. m.	0.94	61.1	15.3	
		1:48 p. m. to 3:07 p. m.	1.30	114.5	11.3	

that the rise in heat production approximately parallels the speed of amino-acid metabolism. This is before the period of maximal nitrogen elimination. Then, too, the sulphur portion of the protein is excreted

24. Lusk, G.: Animal Calorimetry, Paper XI. An Investigation Into the Causes of the Specific Dynamic Action of the Foodstuffs, Jour. Biol. Chem., 1915, **20**, 610.

25. Csonka, F. A.: Animal Calorimetry, Paper X. The Rate at Which Ingested Glycocoll and Alanine Are Metabolized, Jour. Biol. Chem., 1915, **20**, 539.

TABLE 4.—DATA OF CALORIMETER—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calo- rimetry, Cal.	Heat Elimi- nated, Cal.
Case 3 (Saml. G.).. 3/8/16 34.9 Kg. 1.06 Sq. M.	Prelim.	10:14
	1	10:59	13.4	11.9	0.82	19.2	0.261	39.6	40.2
Case 4 (Pat W.)... 3/24/16 37.3 Kg. 1.20 Sq. M.	Prelim.	11:38
	1	12:38	15.7	13.7	0.83	16.1	0.266	46.0	47.1
	2	1:38	17.1	15.8	0.79	17.3	0.266	52.3	50.1
	Aver.
Case 5 (Erwin E.).. 3/6/16 37.4 Kg. 1.17 Sq. M.	Prelim.	12:05
	1	1:05	12.1	10.6	0.83	12.5	0.314	35.3	40.6
	2	2:05	11.9	10.0	0.86	12.5	0.314	33.7	38.0
	Aver.
Case 2 (Geo. F.)... 1/7/16 53.1 Kg. 1.51 Sq. M.	Prelim.	11:40
	1	12:40	16.4	14.0	0.86	16.5	0.309	47.0	51.8
	2	1:40	16.2	15.0	0.79	16.2	0.309	49.6	50.6
	Aver.
Case 8 (S. K.)..... 5/12/16 50.4 Kg. 1.50 Sq. M.	Prelim.	10:50
	1*	11:20	11.5	9.6	0.87	13.0	1.288	31.7	32.5
	2	12:20	26.1	21.2	0.89	23.2	1.288	70.6	66.5
	3	1:20	25.3	22.1	0.83	27.4	1.288	72.3	71.8
	4†	2:30	28.9	25.9	0.81	35.5	1.288	84.4	89.1
	5‡	3:20	19.7	18.6	0.77	25.4	1.288	59.9	62.5
S. K.	Prelim.	10:56
	1	11:56	18.3	16.5	0.81	28.3	0.457	54.8	61.6
	2	12:56	17.9	16.9	0.77	26.1	0.457	55.5	61.2
	Aver.
Case 7 (Robt. L.).. 12/9/14 63.8 Kg. 1.43 Sq. M. (measured)	Prelim.	11:21
	1	12:21	18.2	16.0	0.83	23.5	0.536	53.0	57.8
	2	1:21	21.1	19.0	0.81	24.9	0.536	63.0	65.3
	3	2:21	19.8	18.6	0.77	24.8	0.536	60.9	64.0
	Aver.
Case 6 (Harry J.).. 12/11/14 55.8 Kg. 1.33 Sq. M.	Prelim.	11:06
	1	12:06	20.7	18.8	0.80	23.7	0.419	62.5	59.3
	2	1:06	22.1	18.1	0.89	25.2	0.298	61.6	62.0
	3	2:06	21.9	19.9	0.80	24.5	0.298	66.2	61.3
	Aver.

* 30-minute period.

† 70-minute period.

‡ 50-minute period.

—EXPERIMENTS IN DWARFS AND LEGLESS MEN

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbohyd.	Per Kg.	Per Sq. M. (Lin.)	
.....	36.9	80	Basal; in bed
38.3	36.9	80	11	0.82	18	49	33	1.51	48.9	Quiet, 45 min. period; at 11:32 became nauseated
.....	36.6	Basal; in bed
46.9	36.6	70	15	0.84	15	48	37	Asleep 30 minutes; very quiet
50.9	36.6	79	17	0.79	14	63	23	Awake; quiet
.....	15	55	30	1.32	41.0	
.....	37.3	Basal; in bed
35.0	37.2	61	11	0.84	Very quiet; asleep
35.3	37.1	64	7	0.88	30 min.; read 10 min.
.....	0.86	24	36	40	0.92	29.5	Quiet; no reading
.....	37.0	Basal; in bed
47.1	36.9	59	15	0.87	17	37	46	Quiet; dozed
47.4	36.8	59	16	0.79	17	61	22	Quiet
.....	0.83	17	49	34	0.89	31.1	
.....	36.8	9:15 to 10:12, ate 662 gm. beef containing 24.1 gm.N.
29.9	36.7	67	4	0.95	54	8	38	Very quiet
66.8	36.7	12	0.99	48	2	50	Very quiet
69.5	36.7	69	18	0.86	47	25	28	Very quiet
88.3	36.7	69	26	0.82	47	32	21	Quiet
61.4	36.7	65	0.74	48	46	6	Quiet
.....	36.4	Basal; in bed
53.9	36.2	55	3	0.81	Very quiet; almost motionless
60.9	36.2	55	9	0.76	Very quiet; urinated
.....	22	57	21	1.11	36.8	
.....	36.9	Basal
51.7	36.8	78	8	0.84	27	40	33	Asleep
63.2	36.8	72	22	0.81	23	50	27	Fairly quiet
63.4	36.8	73	19	0.76	23	62	15	Fairly quiet
.....	41.3	
.....	36.8	"Basal"
53.4	36.7	64	13	0.80	18	56	26	1.12	Restless
62.0	36.7	65	16	0.91	13	27	60	1.10	Restless
62.2	36.8	62	13	0.80	12	60	28	1.19	Restless

TABLE 4.—DATA OF CALORIMETER EXPERIMENTS—

Subject, Date, Weight, Surface Area, Linear Formula	Period	End of Period	Carbon Dioxid, Gm.	Oxygen, Gm.	R. Q.	Water, Gm.	Urine N per Hour, Gm.	Indirect Calo- rimetry, Cal.	Heat Elimi- nated, Cal.
Harry J. 5/5/16 54.6 Kg. 1.34 Sq. M.	Prelim.	10:36
	1	11:36	17.8	15.9	0.82	25.6	0.210	53.1	54.2
	2	12:36	18.5	17.4	0.78	24.8	0.210	57.5	55.0
	Aver.
Harry J. 5/10/16 55.8 Kg. 1.34 Sq. M.	Prelim.	11:00
	1	12:00	26.2	23.9	0.80	28.9	1.298	77.9	69.3
	2	1:00	27.1	23.9	0.83	33.7	1.298	78.2	74.8
	3	2:00	27.8	24.0	0.84	40.6	1.298	78.9	81.3
	4	3:00	26.3	23.1	0.83	43.9	1.298	75.6	80.3
Case 1. (Raphael DeP.) 3/15/16 40.9 Kg. 1.24 Sq. M.	Prelim.	11:02
	1§	12:05	18.9	16.8	0.82	22.5	0.603	52.8¶	54.0
	2¶	1:02	16.6	15.0	0.81	20.8	0.603	51.9¶	50.6
	3
Raphael DeP. 3/16/16 40.9 Kg. 1.24 Sq. M.	Prelim.	11:02
	1	12:02	24.6	21.6	0.83	27.8	1.27 (1.88)**	70.8 (69.6)**	63.7
	2	1:02	28.4	24.6	0.84	43.6	1.61 (1.88)	80.5 (79.9)	78.9
	3	2:02	27.1	24.2	0.82	50.6	1.75 (1.88)	78.2 (77.9)	82.6
	4	3:02	26.1	24.5	0.77	50.7	1.88 (1.88)	78.2 (78.2)	81.4
	5	4:02	2.02
Case 9 (G. T. B.)... 5/23/16 54.4 Kg. 1.56 Sq. M.	Prelim.	11:04
	1	12:04	20.8	18.3	0.83	29.5	0.380	61.1	60.6
	2	1:04	20.3	17.9	0.83	28.5	0.380	59.8	63.2
	Aver.
G. T. B. 5/25/16 55.5 Kg. 1.56 Sq. M.	Prelim.	9:55
	1	10:25††	12.4	9.9	0.91	22.6	1.219	33.7	33.3
	2	11:25	27.2	22.8	0.87	42.1	1.219	75.7	76.9
	3	12:25	27.4	24.0	0.83	40.4	1.219	79.0	75.7
	4	1:25	26.7	23.8	0.82	37.4	1.219	78.0	79.3
	5	2:25	27.9	24.9	0.81	40.6	1.219	81.7	84.5

** Figures in brackets based on assumption that the maximum nitrogen excretion represents true protein metabolism for whole experiment.

§ 63-minute period.

¶ Per hour.

¶ 57-minute period.

†† 30-minute period.

—IN DWARFS AND LEGLESS MEN—(Continued)

Direct Calorimetry (Rectal Temp.), Cal.	Rectal Temp., C.	Average Pulse	Work-Adder, Cm.	Non-protein R. Q.	Per Cent. Calories from			Calories per Hour		Remarks
					Protein	Fat	Carbo-hyd.	Per Kg.	Per Sq. M. (Lin.)	
.....	47.7	{ Excluded from averages on account of restlessness
.....	36.7	60	Basal; in bed
49.9	36.6	58	7	0.82	Very quiet; asleep
56.5	36.7	60	7	0.77	30 minutes
.....	0.79	10	68	27	1.01	41.8	Very quiet
.....	36.9	78	{ 8:30 to 9:50 a. m.
68.5	36.9	14	76	0.79	44	40	16	58.1	ate 660 gm. beef
76.3	36.9	16	83	0.85	44	29	27	58.4	containing 24.6 gm. N.
84.9	37.0	22	84	0.88	44	24	32	59.0	Fairly quiet
79.7	37.0	13	83	0.85	46	28	26	56.4	Fairly quiet; voided
.....	36.5	Quiet
52.5	36.5	68	1	0.83	Basal
49.7	36.4	64	1	0.81	Awake; motionless
.....	0.82	31	43	26	1.28	42.2	Awake; motionless
.....	36.9	{ 9:00 to 10:05 a. m.
71.7	37.1	77	4	0.85	47	28	25	1.72	57.1	ate 662 gm. beef
78.8	37.2	83	12	(0.88)**	(72)**	(11)**	(17)**	(1.69)	(56.1)	containing 23.2 gm. N.
81.6	37.2	84	12	0.88	53	19	28	1.96	65.0	Asleep 60 minutes.
78.1	37.1	79	10	(0.90)	(63)	(12)	(25)	(1.94)	(64.5)	Motionless
.....	36.8	0.83	59	23	18	1.90	63.0	Awake; very quiet
63.9	36.9	58	6	0.72	64	34	2	1.90	63.0	Awake; very quiet
63.3	36.9	58	8	(0.72)	(64)	(34)	(2)	(1.90)	(63.0)	Awake; very quiet
.....	Basal; normal control
.....	36.9	Almost motionless
.....	17	47	36	1.11	38.7	Almost motionless
.....	36.9	{ 8:30 to 9:15 a. m.
34.0	36.9	60	0	0.94	24	15	61	ate 600 gm. beef
75.4	37.0	66	12	0.92	43	17	40	containing 23.7 gm. N.
80.3	37.1	64	17	0.85	41	30	29	Motionless
77.5	37.1	64	17	0.82	42	35	23	Almost motionless
85.2	37.1	72	17	0.82	40	37	23	Almost motionless

more rapidly than the nitrogen, as first shown in dogs by Rubner²⁶ and in humans by Wolf.²⁷ Rubner's figures were taken in six-hour periods and show how long continued is the high nitrogen excretion after a meat diet containing 24.7 gm. nitrogen.

The sulphur elimination is shown in Table 2 to be very much more rapid. One would expect the nitrogen to sulphur ratio to be 16, which is that found in meat, but because of the variation in speed of excretion, the ratio falls during the first six hours and is too high in the following periods.

Our observations, which are made in very much shorter periods and extend only to seven hours after food, confirm these findings, except that in the hour during the ingestion of food the nitrogen excretion rises markedly; the sulphur increases but little. This is probably due to the rapid elimination of the extractives in the meat.

This delayed elimination of nitrogen after marked protein ingestion makes its hourly excretion a poor index of the metabolism during that hour. Since the total metabolism stays at a nearly constant level throughout the observation after food, it seems probable that the protein metabolism also stays at a constant level. The same value ought, therefore to be used throughout the observation, not a different one for each hour. The best value to use seems to be the maximum hourly nitrogen excretion and this has been used in all calculations. The effect of this choice is but slight in regard to the height of the total hourly metabolism, but the percentage of calories derived from the three food-stuffs is markedly affected, particularly in the early hours of the observation. This effect can be seen in Table 4, in which, in the case of R. De P., the calculations are made in both ways: (1), using the N as excreted; and (2), using the maximum value as the hourly excretion. The figures for Louis M. will be found in Paper 4 of this series.

The tables show quite clearly that no matter which value is assumed as the true protein metabolism, in the first hours of the observation a large part of the specific dynamic action is at the expense of the oxidation of carbohydrates. This is true of all cases except that of Louis M., in whom the 100 gm. of fat taken with the meat probably affected the relationship. This finding is not in accord with the results of Gigon.²⁸ He used casein and found that the specific dynamic action was due to protein metabolism alone, and that carbohydrate and fat were even spared slightly. Gigon's results on the increased heat production fol-

26. Rubner, Max: *Die Gesetze des Energieverbrauchs bei der Ernährung*, Leipzig, 1902, p. 369.

27. Wolf, C. G. L.: *Die Ausscheidungszeit von Stickstoff, Schwefel und Kohlenstoff nach Aufnahme von Eiweisssubstanzen und Spaltungsprodukten*, Biochem. Ztschr., 1912, **40**, 234; *ibid.*, 1912, **41**, 111.

28. Gigon, A.: *Ueber den Einfluss der Nahrungsaufnahme auf den Gaswechsel*, Arch. f. Physiol., 1911, **140**, 509.

lowing casein ingestion are of interest in relation to the percentage increase which we have found. The results obtained by Gigon were recalculated by Williams, Riche and Lusk,²⁰ and the chart of their findings is here reproduced (Table 5). It shows an average specific dynamic action (70) which is lower than that reported in this paper (76). This difference is possibly due to the different form of protein ingested.

Stachelin²⁹ obtained, in one observation, results which are quite different from those of Gigon or from those here reported. He used a Jaquet apparatus, determining the metabolism in two hourly periods. The test meal consisted of 75 gm. of protein and 12.2 gm. of fat. In the twelve-hour observation following the meal the urine nitrogen increased 0.37 gm. per hour, which represents 9.9 calories of increased protein metabolism. The respiratory observation, however, indicates

TABLE 5.—INCREASE OF METABOLISM IN MAN DUE TO PROTEIN INGESTION (GIGON)

Food Casein, Gm.	Increase in Protein Metabolism		Increase in Total Calories of Metabolism	100 Calories of Protein Metabolism Increases Total Calories by
	Gm.	Calories		
50	7.1	28.4	19	67
100	23.8	95.2	58	56
150	35.7	142.8	118	88
200	58.1	232.4	171	74
Average.....				70

an average increased elimination by the body of 24.6 calories per hour and an increase in the proportion of fat metabolized. This result is not in accord with the other experiments here recorded.

Another conclusion may be drawn from the observations as viewed in Table 6. The relationship between the normal and abnormal cases shows that the specific dynamic action did not follow the surface area. The three normal cases have values per square meter which are very close together. The percentage increase of the two abnormal cases, however, is distinctly higher, which shows that diminishing the surface area or muscle volume did not proportionally reduce the intensity of the specific dynamic action. In the last column of the chart is shown the total percentage increase, found by dividing the actual increase in metabolism by the calories of extra protein oxidized. If one allows for the increased heat due to the fat ingestion of Louis M., the ratios

29. Stachelin, R.: Versuche ueber Gaswechsel und Energieverbrauch nach Nahrungsaufnahme, Ztschr. f. klin. Med., 1908, **66**, 201.

are all closely related. We interpret this to mean that the specific dynamic action is dependent in these cases on the total protein metabolism. It is certainly independent of the mass of muscle tissue.

NORMAL CONTROLS

In the course of these experiments and of those recorded in Paper 20 of this series there have been six basal observations on normal men between the ages of 23 and 34. Four are new subjects whose metabolism has not been previously determined.

The basal metabolism of E. F. D. B. was determined four times in the spring of 1913, when an average value of 39.8 calories per square meter per hour was found. In May, 1915, the metabolism by the same index was 37.6 calories. In May, 1916, the height of his metabolism was 38.4 calories. This shows the constancy of the basal metabolism of some normal individuals.

TABLE 6.—SPECIFIC DYNAMIC ACTION. PERCENTAGE INCREASE

Name	Physical Condition	Urinary Nitrogen		Calories Extra Protein Metabolized per Hr. Extra N $\times 26.5$	Actual Calories Increase per Sq. M. per Hr.	100 Calories of Protein Metabolism Increases Cals. per Sq. M. by	Actual Total Calories Increase per Hr.	100 Calories of Protein Metabolism Increases Total Calories by
		Basal, per Hr.	After Meat, per Hr.					
R. DeP.	Achondroplasia	0.60	1.88	33.9	19.4	57.2	24.1	71.1
Harry J.	Legless man	0.21	1.30	28.9	16.6	57.5	22.3	77.2
Louis M.*	Normal control	0.52	1.14	16.4	8.3	50.5	15.3	93.1*
W. B.	Normal control	0.38	1.22	22.3	11.7	52.6	18.2	81.8
S. K.	Normal control	0.46	1.29	22.0	11.1	50.5	16.6	75.5

* Regular protein meal plus 100 gm. of fat.

The metabolism of J. H. M. had been determined by the Benedict unit apparatus and reported in the series of Palmer, Means and Gamble,³⁰ and of Means.² The average of these observations is 39.4 calories per square meter per hour. These findings were made more than a year before our determination (39.5 calories) and on a different type of apparatus.

The average calories per square meter per hour of these six controls is 38.9. The average found in this laboratory for normal men between the ages of 20 and 50 is 39.7 calories per square meter per hour. The six controls reported here average 2 per cent. below this figure (Table 7).

30. Palmer, W. W., Means, J. H., and Gamble, J. L.: Basal Metabolism and Creatinin Elimination, Jour. Biol Chem., 1914, **19**, 239.

TABLE 7.—SUMMARY OF BASAL METABOLISM OF SIX NORMAL CONTROLS. MEN

Name	Date	Age	Height, Cm.	Weight	Surface Area, Sq. M. Linear Formula	Calories per Sq. M. per Hour	Variations from Average Normal 39.7 %	Average R. Q.	Total Calories Measured		Divergence of Direct from Indirect, per Cent.
									Indirect	Direct	
E. F. D. B.	4/12/16	34	179.5	76.47	1.94	38.8	-2.2	0.80	150.71	161.79	+7.4
	4/25/16*	1.95	37.6	-5.4	0.80	73.23	71.54	-2.3
J. H. M.	4/21/16	30	177.0	75.34	1.89	38.5	-0.6	0.86	149.12	155.04	+4.0
J. C. F.	4/27/16	23	178.0	64.29	1.75	41.7	+5.1	0.82	146.05	149.18	+2.2
J. C. A.	4/29/16	26	175.2	60.20	1.64	39.2	-1.3	0.86	123.46	149.49	+16.3
S. K.	5/16/16	33	161.5	49.53	1.50	36.8	-7.4	0.79	110.31	114.84	+4.1
G. T. B.	5/23/16	25	164.5	54.37	1.56	38.7	-2.4	0.83	120.87	127.17	+5.2
Average.....	38.7	-2.4	+5.7

* One hour experiment. All others two hours.

SUMMARY

1. The basal metabolism of five dwarfs, two legless men and six normal controls is reported. The legless men and the dwarfs, with apparently normal endocrine systems, showed, in relation to their surface area, the same level of metabolism as normal men. The law of surface area holds good for men of unusual body shape.

2. The dwarfs with involvement of the ductless glands and symptoms of cretinism showed a marked reduction in metabolism below the average found in normal cases, as has been reported by other authorities.

3. Following the ingestion of large quantities of meat, the excretion of urinary nitrogen during the earlier hours is not an accurate index of the protein metabolism. The sulphur excretion is more rapid than the nitrogen excretion.

4. The stimulation of metabolism following a large amount of meat is almost at its height two hours after the meal is eaten. The extra heat produced may amount to three-quarters of the calories in the protein metabolized, and may lead to an increase of 46 per cent. above the level of the basal heat production.

5. The specific dynamic action of a meal containing 24 gm. of nitrogen in the form of meat was larger in the case of a legless man, and of an achondroplastic dwarf, with very small arms and legs and normal trunk, than in the cases of three normal controls of greater weight and greater surface area. This indicates that the intensity of the specific dynamic action is not proportional to the mass of the musculature. The true explanation of the results cannot be given in the light of present knowledge. Various possible explanations come naturally to mind, such, for example, as a greater concentration of amino-acids in the blood flowing to the muscles, or the presence of a liver, which, in proportion to the size of the organism, is relatively larger than the normal.

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