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ENERGY EXPENDITURE IN MAN

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The development of experimental methods for determining the energy expenditure of man

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The proof by Lavoisier (1775–85) of the true nature of oxidation, his demonstration that in respiration oxygen was used up and CO_2 produced, and in greater quantity during muscular movement and after food, and his conclusion that the heat of the body was essentially a slow combustion involving the oxidation of carbon to CO_2 and hydrogen to water, gave an immediate clue to the means by which an estimate might be made of the varying energy output of the living animal. An index of it could be derived from the products of the oxidation, the amount of oxygen consumed or the rate of loss of heat from the body. In tracing the development of methods for this purpose space will only allow me to select instances which appear to me to have played an important part in advancing our knowledge, and, omitting intervening years, I shall start with the experiments of Regnault & Reiset (1849). Animals (rabbits, dogs, birds) were placed in an air-tight bell jar which was sunk in a water-bath the temperature of which could be easily controlled. The CO_2 produced by the animal was removed by potassium-hydroxide solution in a pump which constantly removed air from the chamber and returned it, the carbonate formed being estimated subsequently, and the deficiency of oxygen was made good by automatically admitting oxygen so as to maintain a constant pressure within the bell jar. The apparatus therefore worked on the closed system and is the prototype on which many apparatuses have been based up to the present day. Apart from the actual figures for the respiratory exchange Regnault & Reiset's results were regarded as compatible with the assumption that the metabolism did not result in the formation of any free nitrogen: if so, the protein metabolism could be gauged from the nitrogen excretion in the urine and faeces. The actual figures were, however, rather irregular, and 57 years elapsed before Krogh (1906) was able to prove convincingly that this view was correct in what are probably the most elegant and accurate experiments ever made with an apparatus of the Regnault-Reiset type.

Edward Smith (1859*a*,*b*) designed a portable open-circuit apparatus for experiments on man in which the subject fitted with a valved facepiece inspired ordinary air through a dry-gas meter. The expired air was directed through a bottle containing pumice soaked in strong sulphuric acid to remove water vapour, and then

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through a canister where it came into contact with potassium-hydroxide solution to absorb CO_2 the amount of which was ascertained from the gain in weight of the canister. With this apparatus he made experiments both during rest and when walking at 2 and 3 m.p.h. He did not measure the oxygen consumption. The figures which he gives for his own CO_2 production are precisely the same as I found on myself half a century later by the bag method, which may perhaps suggest that not much progress had been made in the interval.

Pettenkofer (1862) fearing that a mask or mouthpiece and respiratory valves might interfere with the natural breathing, and obsessed with the idea still prevalent that some odorous and possibly toxic volatile substances might be given off in the expired air and accumulate in a closed system to the prejudice of the subject, built a metal-lined respiration chamber of 12·7 m^3 (450 ft^3) capacity the cost of which was borne by King Maximilian II of Bavaria. This chamber was ventilated by drawing fresh air through it by a pump; its volume could be varied between 15 and 75 m^3/h and was measured by a gas meter. A sample of the air leaving the chamber was passed through sulphuric acid to remove water vapour, barium-hydroxide absorption tubes to remove CO_2 and a small gas meter to measure the actual volume. The CO_2 production could thus be determined. Voit (1875) used an apparatus designed on the same principle for small animals save that the main ventilating current was secured by mechanically rotating the drum of a wet-gas meter.

Hoppe-Seyler (1894) designed a respiration chamber for man on the same principle as that used by Regnault & Reiset and employing the same type of potassium-hydroxide pump. The capacity of this chamber was 4·8 m^3 (170 ft^3), and with it he could determine the oxygen consumption as well as the CO_2 production.

Further large human respiration chambers on the open-circuit system were built by Sondén & Tigerstedt (1895) of 100 m^3 (3500 $ft.^3$) capacity in Stockholm, and by Tigerstedt (1906) of 76 m^3 (2700 $ft.^3$) capacity in Helsinki. In the former instance ventilation was secured by pump and gas meter, in the latter by mechanical rotation of the drum of a wet-gas meter. In both instances CO_2 concentration, but not that of oxygen, in the aliquot sample taken from the air leaving the chamber was determined by the apparatus of Petterson & Sondén (1895) for the accurate analysis of CO_2 in air. It was with the chamber in Helsinki that Becker & Hämäläinen (1914) made their observations on the daily output of energy by persons of different occupations. Zuntz had built by the beginning of this century a respiration chamber of 80 m^3 (2800 $ft.^3$) capacity in the Landwirtschaftliche Hochschule in Berlin which he used for determining both the CO_2 output and oxygen intake, on the Regnault-Reiset principle, of the larger domestic animals (such as horses, cattle) in a long series of nutritional studies. A detailed description is given by von der Heide, Klein & Zuntz (1913), and will give a good idea of the complicated construction of a large respiration chamber at this date.

Jaquet (1903) used an open-circuit method in which pure air was drawn by a pump through a chamber of 1·4 m^3 (50 $ft.^3$) capacity, in which the subject could sit or lie, and through a wet-gas meter, a small sample being taken from the air leaving the chamber at a rate governed by the rotation of the drum of the meter, the CO_2 and oxygen content being determined in this by an apparatus of the Petterson type. In the small open-circuit chamber built by Grafe (1910) the sides fitted into a water seal in the floor, and a door was abolished since the whole chamber could be lifted to admit the subject. The main ventilating current was ensured by the mechanical rotation of a wet-gas meter. On the basis of these last two methods Krogh & Lindhard (1920) constructed the open-circuit chamber of 2·27 m^3 (80 $ft.^3$) capacity which allowed work to be done on a bicycle ergometer in their investigation of the relative value of fat and carbohydrate as sources of muscular energy. As the CO_2 concentration in the air leaving the chamber was not allowed to rise to more than about 0·5% Krogh designed a volumetric gas-analysis apparatus accurate to 0·001%.

Although Lavoisier & Laplace (Lavoisier, 1775–85) had measured the heat output of an animal by means of an ice calorimeter it was not until D'Arsonval (1886) described his differential calorimeter that a satisfactory method for animal calorimetry became available. Rubner (1894) used this differential principle in the apparatus with which he made his classical comparison of the heat given out by a dog with that calculated from the CO_2 and water output and the nitrogen excretion as indices of the substances oxidized in the body, thus proving that the principle of the conservation of energy holds good in the living body and justifying the indirect calculation of the energy output. These conclusions have been fully confirmed by numerous experiments made on man during both rest and muscular exercise with the respiration calorimeter of Atwater & Benedict (1905) in which the calorimeter chamber also serves as a closed-circuit respiration chamber on the Regnault-Reiset principle. This apparatus is so well known that I need not describe it in detail. Other calorimeters for animals, whether small or large, have been designed by Hill & Hill (1913, 1914) and by Capstick (1921). The most recent design for a human calorimeter has been suggested by Benzinger & Kitzinger (1949). In this the wall of the calorimeter chamber is formed of a material of known thermal conductivity and uniform thickness which is a non-conductor of electricity. A very large number of thermocouples are distributed over the sides, roof and floor, the warm junctions being on the inner surface and the cold on the outer. By joining the thermocouples in series an integrated record of the average gradient of temperature between the outer and inner surfaces can be secured. A method almost identical with this has been successfully used during the last few years in the large calorimeter chambers in which the efficiency of space-heating appliances is assessed at the Fuel Research Station of the D.S.I.R.

Respiration chambers are suitable for experiments of long duration, but information about human energy output can very often be satisfactorily obtained in experiments of short duration. One instance, Edward Smith's method, has already been described. Geppert and Zuntz in 1887 introduced an open-circuit apparatus of which the best description was given by Magnus-Levy (1894). In it the subject breathed through a mouthpiece and respiration valves, the expired air being directed through a wet-gas meter. As the drum of this gas meter rotated, a gearing on its shaft lowered the outlet tube of a gas burette which had been filled at the beginning with liquid: the burette was therefore gradually filled with a proportional fraction from each successive expiration, and analysis of this composite sample and the total volume recorded by the meter allowed the respiratory exchange to be calculated. The original form of this apparatus was only suitable for the laboratory, but for field observations the wet-gas meter was replaced by a dry meter which could be carried on the back, and this form was used in an extensive series of observations during rest and exercise by Zuntz, Loewy, Müller & Caspari (1906) and by Durig, Kolmer, Rainer, Reichel & Caspari (1909) in their expeditions to Monte Rosa. Although this method fell into the background in subsequent years it was resuscitated with a trifling modification by Kofrányi & Michaelis (1940) and has been used for field observations in recent years. The short-period apparatus designed by Benedict (1912), which was so extensively used in the investigations during rest and exercise made in the Nutrition Laboratory of the Carnegie Institution of Washington, is essentially a pipe circuit round which air is driven by a blower, the subject breathing back and forth into this circuit while water vapour and CO_2 are absorbed and oxygen deficiency compensated on the Regnault-Reiset principle.

I need not describe the bag method which I introduced (Douglas, 1911); it has proved very successful in practice for short-period work, for it is simple to operate, readily adaptable to a great variety of conditions and has the advantage of portability. Nor need I refer to the spirometer units which have been so much used in clinical practice: in most instances these only afford a graphic record of the rate of consumption of oxygen, but in the final form developed by Fleisch (1954), and named by him the Métabographe, a very ingenious, though complicated, closed-circuit apparatus allows a graphic record to be obtained by mechanical means of the respiratory volume, CO_2 output, oxygen absorption and R.Q.

Hanriot & Richet (1891) designed a method for determining the respiratory exchange which employed three moderately large wet-gas meters but this apparatus, like the large spirometers used by Speck (1892) and Tissot (1904), had the disadvantage of being too cumbrous.

The calorimeter has done its main work in justifying the indirect method for estimating the energy output, although it may still have a part to play in settling some uncertainties, but the indirect method is not only simpler but affords information about the sources from which the energy liberated in the body is derived. In the open-circuit chambers in which CO_2 output alone was directly measured the oxygen consumption of the subject could only be gauged from the difference between the initial weight of the subject + the measured ingesta and the final weight of the subject + the measured excreta. The value thus calculated could never be very exact since there was always uncertainty about the water vapour which might have been adsorbed on the objects in the chamber. Far more certain results were obtained when they were based on the analysis of the CO_2 and oxygen content of the air leaving the chamber.

Short-period experiments have been successfully used for integrating the energy output of the different daily activities so as to ascertain the energy output over 24 h in order to assess the nutritional requirements, laborious though the method may be.

A respiration chamber might seem to offer advantages for this purpose, but there are many forms of natural activity which cannot be adequately represented in such a chamber. An alternative is to base our estimate of the energy output on the food intake during the 24 h.

Most of the methods for determining the respiratory exchange involve volumetric gas analysis by chemical methods (which can be done extremely accurately) but gravimetric methods have been used in some instances. In more recent years, however, new physical methods of gas analysis have been introduced, for example the katharometer (Daynes, 1920); methods depending on the differential passage of a gas mixture through a divided capillary resistance when one of the component gases is absorbed in one limb of the resistance (Rein, 1933); the nitrogen meter (Lilly, 1946); the paramagnetic oxygen meter (Pauling, Wood & Sturdivant, 1946); the infra-red analyser (Fowler, 1949); the adaptation of the mass-spectrometer to respiratory problems (Hitchcock & Stacy, 1948). Such physical methods are in themselves excellent, although some may analyse only CO_2 and others only oxygen content, but in the indirect method for estimating the respiratory exchange the gas-analysis apparatus is but a means to an end, and if these newer methods are to supplant the older chemical analysis they must offer some advantages without sacrifice of accuracy, for example greater ease and speed of analysis. The cost of the apparatus is also a matter for serious consideration. There are occasions when it is necessary in physiological investigations to secure and analyse at once a rapid succession of air samples in order to guide the course of an experiment, and here is clearly a case for a physical method. Again with the mass-spectrometer it is possible to record the simultaneous changes of both CO_2 and oxygen concentration in the expired air in a succession of breaths during natural breathing, and if these observations can be extended to cover the breathing during moderate and severe muscular exercise the results will probably go far towards settling certain controversial questions about the regulation of the breathing during exercise, but if I continue on this line I may rightly be accused of straying from the true course of our discussion.

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Modern techniques for measuring energy expenditure

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All instruments measuring energy expenditure by indirect calorimetry must have the following functions. They must measure the volume of air expired over a given time, and produce a sample representative of the whole experimental period.

The Douglas bag (Douglas, 1911) is a special instance of such an 'instrument' in which all the air is collected and is available for subsequent analysis and volume measurement. It is just those qualities which make the Douglas bag an absolute method for laboratory work that militate against its employment in the field.

It has become customary in recent years to attempt to follow the energy expenditure of people over long periods with a view to establishing either a calorie balance-sheet of input against output, or to assess the 'hardness' of a given employment or task.

For such an investigation long-term measurements have to be carried out under conditions of minimal interference with normal activity.

The qualities which a suitable instrument must possess are the following:

(1) The weight and the resistance to respiratory air flow must be sufficiently low to impose only a negligible physiological load, both subjectively and objectively.

(2) The integrated sample produced at the finish must be as similar as possible in composition to the mixed contents of a very large Douglas bag, if such had been used.