J. Physiol. (1968), 199, *pp.* 685–703
With 11 *text-figures*
Printed in Great Britain

OXYGEN CONSUMPTION IN NORMALLY GROWN, SMALL-FOR-DATES AND LARGE-FOR-DATES NEW-BORN INFANTS

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(*Received* 22 *July* 1968)

SUMMARY

1. Serial measurements of minimal oxygen consumption ($\dot{V}_{O_2}$) have been obtained from nineteen healthy new-born infants in order to find out how body weight, gestational age and age after birth affected $\dot{V}_{O_2}$. The first measurement of $\dot{V}_{O_2}$ was done within 12 hr of birth, and further measurements were made at intervals until the baby left hospital.

2. The majority of the infants (seventeen) weighed less than 2·5 kg at birth, and were 'premature' according to international definition. Gestational age, calculated from the mother's last menstrual period, was corroborated by clinical data and obstetrical history. The babies were divided into four groups according to birth weight and gestational age combined (see Table 1). Babies in the first two groups were the appropriate weight for dates (i.e. normally grown), babies in the other two groups were either small-for-dates or large-for-dates.

3. At birth minimal $\dot{V}_{O_2}$ was closely correlated with birth weight in all babies and appeared to be directly proportional to it. The value for $\dot{V}_{O_2}$/kg was similar in all groups. $\dot{V}_{O_2}$ was not related to gestational age *per se*. However, in the two normally grown groups $\dot{V}_{O_2}$ was roughly related to gestational age because birth weight was related to gestational age.

4. In all babies minimal $\dot{V}_{O_2}$ rose progressively with increasing age after birth; a marked increase in $\dot{V}_{O_2}$ occurred in the first week of life, despite a small decline in body weight.

5. At a given age after birth differences in $\dot{V}_{O_2}$/kg between the four

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groups were mostly less than 10 %, and in general the differences were not statistically significant.

Values for minimal $\dot{V}_{O_2}$ in all four groups were roughly:

5 ml. O_2/kg.min at < 12 hr of age.
7 ml. O_2/kg.min at 7–14 days of age.
9 ml. O_3/kg.min at about 2 months of age.

6. It is concluded that:

(*a*) At birth minimal $\dot{V}_{O_2}$ is largely determined by birth weight. $\dot{V}_{O_2}$/kg is little affected by either rate of growth *in utero* or gestational age.

(*b*) Minimal $\dot{V}_{O_2}$ is a function of age after birth as well as of body weight, and the value for $\dot{V}_{O_2}$/kg increases as the baby gets older.

INTRODUCTION

The growth rate of babies *in utero*, as estimated from birth weight at known gestational ages, varies widely (Lubchenco, Hansman, Dressler & Boyd, 1963; Butler & Bonham, 1963). In deciding what is abnormal a major difficulty is that neither age, nor weight, considered independently, provides a satisfactory criterion of 'prematurity'. For example, the Perinatal Mortality survey (Butler & Bonham, 1963) found that nearly 40 % of babies classed as premature according to international definition, which is based purely on weight (less than 2·5 kg at birth), have gestational ages of 38 weeks or more, and would generally be held to be mature from the age standpoint. However, these small-for-dates babies undoubtedly constitute a special high-risk group, since their mortality is some eight times higher than that of babies weighing more than 2·5 kg at birth, who also have gestational ages greater than 38 weeks. Small babies between 1·5 and 2·0 kg in fact have a higher mortality when their gestational age is 36 weeks or more than when it is 30–35 weeks (McDonald, 1965). The importance of distinguishing between low birth weight due to short gestation and that due to retarded intrauterine growth is clear; investigations in which this distinction is made should lead to a better understanding of the situation and its post-natal consequences.

The investigation reported here concerns oxygen consumption in a sample of babies who weighed 2·5 kg or less at birth and whose gestational age was accurately assessed; minimal oxygen consumption was measured as soon after birth as possible and the measurement was repeated at intervals as the baby got older. Two babies who were immature by gestational age, yet large-for-dates, are included to provide a contrast. The data were analysed to find out to what degree minimal oxygen consumption at birth was determined by body weight and to what degree by gestational age.

The data obtained at increasing age after birth were also analysed in an attempt to discover the relative roles played by age after birth and by body weight in determining the oxygen consumption.

METHODS

The investigations described below were harmless to the babies, and no infant showed any untoward effects that could be attributed to the investigative procedure, either at the time or subsequently. The purpose of the investigation, and the procedure, were explained to each mother, who was then free to decide whether to permit her infant to take part in the investigation. All the babies in this series, save three who were born by Caesarean section and are referred to later, were born normally by vaginal delivery. Only babies who showed no clinical evidence of cardiac or respiratory disease, nor signs of asphyxia during or after birth, and who did not suffer from hyperbilirubinaemia, are included in this report: all infants stayed healthy and asymptomatic throughout the period of study.

Apparatus and experimental details

Oxygen consumption rate was measured using the apparatus described in detail by Hill & Rahimtulla (1965): the differentiating float was capable of recording accurately oxygen consumption rates as low as 4 ml./min and the apparatus was sensitive enough for even the smallest premature infant. The investigations were done during an interval between feeds (the babies being fed 3-hourly, or occasionally 2-hourly), so that the feeding routine was not disturbed in any way. The experimental procedure that was followed has been described by Hill & Rahimtulla (1965): at each investigation oxygen consumption was measured over a period of approximately 10 min, at a number of different environmental temperatures, both at temperatures judged to be within the thermoneutral range of temperatures and also in 'cold' conditions. Similarly to what emerged from the previous study, all the babies in this series showed an increased oxygen consumption in 'cold' conditions; however, we shall not be dealing with the metabolic response to cold in this paper. All the measurements reported here were obtained while the baby was inactive or sleeping, breathing air of approximately normal composition, and in an environment that was thermally neutral for the baby concerned, thus all values reported here are approximately minimal values (or in older terminology basal or standard values). (Environment in baby-chamber for thermoneutrality: dry bulb temperature in the region of 36° C (extreme range 32–40° C, depending on the baby's size and age), radiant temperature within 2° C of dry bulb temperature, relative humidity 20–25 %: volume flow of circulating air 25 l./min, with a linear flow through the baby-chamber of 2–3 cm/sec.)

From every investigation generally two or more estimates of minimal oxygen consumption were obtained; in calculating the final results these estimates were pooled and mean values are given: all volumes are expressed at s.t.p.d.

Rectal temperature was monitored continuously while oxygen consumption was being measured; where rectal temperature changed slightly over a given period of $\dot{V}_{O_2}$ measurement, the mean value has been used in the final results.

Symbols used throughout the paper are:

$\dot{V}_{O_2}$ = minimal oxygen consumption, ml./min,
T_R = rectal temperature, °C,
W = body weight, kg.

The babies

Each baby was investigated repeatedly until it left hospital. Such repeated measurements were obtained from nineteen babies who either weighed less than 2·5 kg at birth or had been born before term (representing a total of 275 measurements of oxygen consumption obtained from 130 separate investigations).

Gestational age. This was carefully assessed in each baby. It was calculated from the first day of the mother's last menstrual period as stated in the antenatal notes, and is given in weeks (to the nearest week). Consideration was also given to:

(i) The size of the uterus at the first obstetrical examination (generally at 12–16 weeks) as recorded in the antenatal notes.

(ii) The clinical appearance and behaviour of the infant at birth.

(iii) The obstetrical history, including any relevant clinical details.

In all the babies in the sample the clinical criteria (i), (ii) and (iii) corroborated the gestational age as calculated from the mother's last menstrual period. One additional baby who would otherwise have been included in the sample was rejected because of uncertainty over the date of the mother's last menstrual period.

Age after birth. Each baby was examined at a number of different ages: it was not practicable to do the investigations at precisely the same age for each baby, but we did succeed in making the first measurement within 12 h of birth in almost every case. Babies who were healthy and thriving were discharged 10–14 days after birth provided that their weight was not much below 2·5 kg. Babies of considerably lower weight were kept in hospital until their weight had reached this value, and we were able to follow them for very much longer: the shortest stay was 10 days, the longest 10 weeks. In order to analyse for a possible effect of age after birth, we found it necessary to define age classes which were arbitrarily chosen as follows:

Class	I	II	III	IV	V	VI	VII
Age	< 12 hr	12–48 hr	2–7 days	7–14 days	2–4 weeks	1–2 months	> 2 months

RESULTS

Birth weight in relation to gestational age. Birth weight is shown plotted against gestational age for all nineteen babies in Fig. 1. The 90th, 50th and 10th percentiles derived from the Denver study of birth weight in relation to gestational age (Lubchenco *et al.* 1963) are indicated, and also the mean birth weight ± 1 S.D. for the later weeks of gestation from data of the National Birthday Trust Perinatal Mortality Survey (Butler, 1965). Each baby in our sample (with a single exception, described in detail later) could be assigned to one of four well-defined groups according to birth weight and gestational age combined, namely:

(1) Young pre-term (indicated by filled triangles).
(2) Pre-term (indicated by filled circles).
(3) Small-for-dates (indicated by open squares).
(4) Large-for-dates (indicated by open diamonds).

These symbols will be retained in most of the figures that follow. Note that filled symbols have been used where the baby's weight was within ± 10th percentile limits for gestational age (normally grown), open symbols where weight was either below the 10th or above the 90th percentile limit for gestational age (small-for-dates and large-for-dates). Table 1 gives further details about the grouping.

The weight of all young pre-term and pre-term babies fell within the 90th and 10th percentile limits and they were judged to be of appropriate weight for gestational age: these babies are termed 'normally grown' (cf. Sinclair & Silverman, 1966). Small-for-dates babies fell well below the

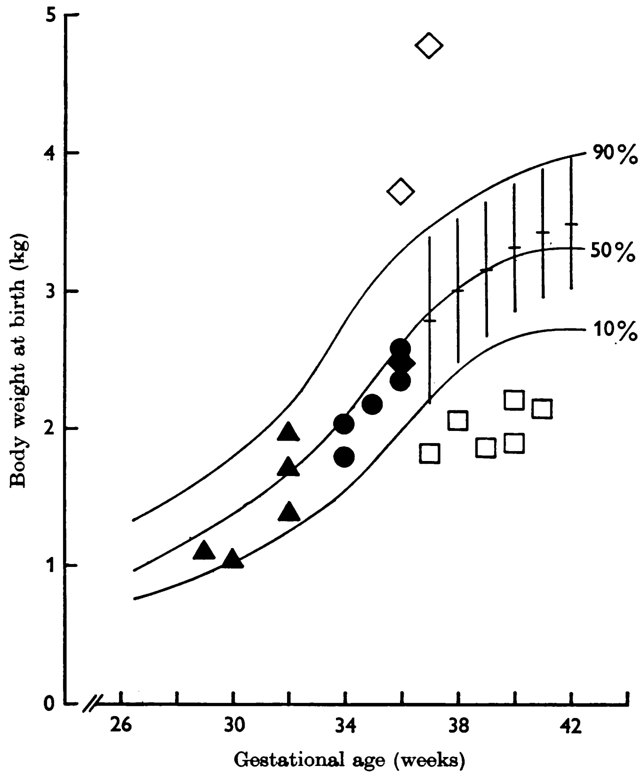

Fig. 1. Ordinates: Birth weight, kg. Abscissae: gestational age, weeks. Triangles: young pre-term. Circles: pre-term. Squares: small-for-dates. Diamonds: babies of diabetic mothers; two are large-for-dates, see text.

The symbol has been filled in when the baby's weight is appropriate to its gestational age, and has been left open when the weight is either lower or higher than usual for gestational age, i.e. open for small-for-dates and large-for-dates.

The three curved lines indicate the 90th, 50th and 10th percentiles from data of Lubchenco *et al.* (1963) for babies of both sexes. The horizontal bars with associated vertical line indicate respectively, the mean birth weight, ± 1 S.D., for each completed week of gestation from 36–41 from data of the Perinatal Mortality survey (Butler, 1965).

10th percentile and all clearly weighed less than the norm. The mothers of the remaining three babies were all diabetic, and for this reason all three were delivered by elective Caesarean section before term (at 36–37 weeks gestational age). Two were characteristically 'large-for-dates', their weight being above the 90th percentile limit. The third baby was not large-for-dates, in fact its weight was just below the 50th percentile for its gestational age. We decided that for purposes of statistical analysis we should not include this infant with the pre-term group, even though it had the weight-for-gestational age characteristics of this group. This baby, therefore, has been given a special symbol of its own (filled diamond) so that it can be distinguished from pre-term babies among whom it lies in Fig. 1.

Rectal temperature. Body temperature might be expected to affect $\dot{V}_{O_2}$, so before comparing $\dot{V}_{O_2}$ values in the different groups of babies it was

TABLE 1. Sample broken down into groups

Birth wt.	Size for dates	Maturity	Group description and symbol	Gestational age	Birth wt. mean and S.D.	n*
Low	Normal	Very immature	Young pre-term ▲	29–32 weeks	1·47 kg ± 0·39	5
Low	Normal	Immature	Pre-term ●	33–36 weeks	2·19 kg ± 0·30	5
Low	Small	Mature	Small-for-dates □	37–42 weeks	2·0 kg ± 0·16	6
High	Large	Immature	Large-for-dates ◇	36, 37 weeks	3·71 kg & 4·78	2

* The remaining baby who makes up the full total of nineteen could not properly be assigned to any one of these groups (its mother was diabetic, yet it was not large-for-dates. 36 weeks, 2·47 kg). In the figures it has been given a special symbol of its own: see text.

necessary to find out whether rectal temperature, recorded during each period of $\dot{V}_{O_2}$ measurement, varied significantly between the groups. Table 2 shows the results of statistical analysis of rectal temperature values (the number of babies in the 'diabetic' group was too small for statistical analysis so individual values are given). At a given age the more immature babies tended to have a lower rectal temperature than the mature ones, but the difference between the mean values for the various groups was small, never more than 1° C at a given post-natal age, which is not statistically significant. In view of the fact that a difference in rectal temperature of this order could theoretically affect $\dot{V}_{O_2}$ values by only a few percent at the most, rectal temperature has been ignored in analysing the $\dot{V}_{O_2}$ results; however, the variation may well have contributed somewhat to the scatter of the individual measurements.

$\dot{V}_{O_2}$ *at birth*

$\dot{V}_{O_2}$ in relation to gestational age. The results obtained are shown in Fig. 2. It is seen that $\dot{V}_{O_2}$ and gestational age are well correlated in normally grown infants, but small-for-dates and large-for-dates babies mostly lie nowhere near the same line as the normally grown ones. Thus $\dot{V}_{O_2}$ at birth does not appear to be dependent on gestational age *per se*.

V_{O_2} *in relation to birth weight.* Fig. 3 demonstrates the results obtained. The continuous line is the regression of $\dot{V}_{O_2}$ at 0–12 hr after birth on body weight, calculated from data for normally grown babies only (i.e. young pre-term and pre-term together, making ten pairs). The correlation

TABLE 2. Mean rectal temperature, ±1 S.D. followed by n, by group and age class

Group	Age after birth < 12 hr	12–48 hr	2–7 days	7–14 days
Young pre-term	35·6 ± 0·65 5	35·8 ± 0·54 5	35·9 ± 0·38 5	36·2 ± 0·34 5
Pre-term	35·8 ± 0·79 5	36·3 ± 0·24 5	36·7 ± 0·59 5	36·5 4
Small-for-dates	36·3 ± 0·55 5	36·6 ± 0·22 5	36·8 ± 0·34 5	36·6 5
Diabetic mother	36·2	36·5	37·1	
(individual	37·0	36·9		37·0
values)	36·3	37·0	37·2	

The individual values used in calculating mean and S.D. are derived from values observed during periods over which $\dot{V}_{O_2}$ was measured, as shown in Table 3: at every age a given baby contributes only one value.

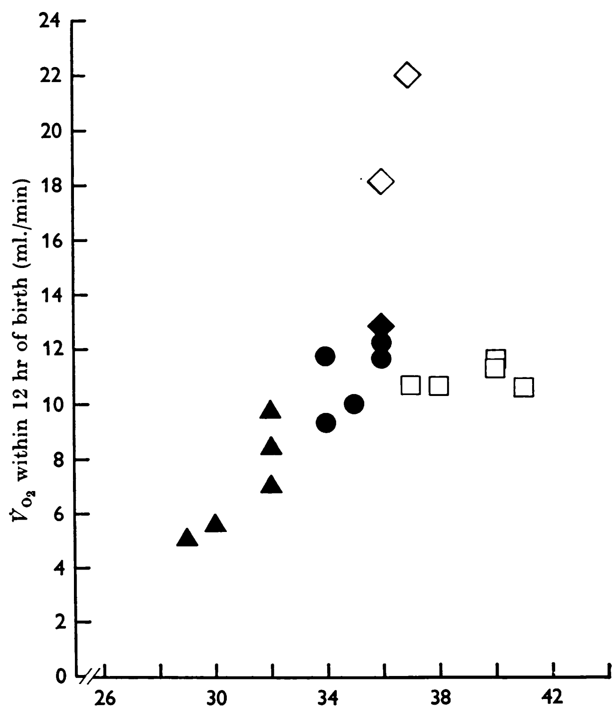

Fig. 2. Ordinates: $\dot{V}_{O_2}$, ml./min, measured within 12 hr of birth. Abscissae: gestational age, weeks. Symbols and shading as in Fig. 1.

coefficient is high, $r = 0{\cdot}96$, $P < 0{\cdot}001$: also the regression line passes close to the origin, equation

$$\dot{V}_{O_2}\ \text{ml./min} = 4{\cdot}81 \times W\ \text{kg} + 0{\cdot}32.$$

For practical purposes the small intercept is best disregarded: $\dot{V}_{O_2}$ is then directly proportional to body weight as shown by the pecked line which has been drawn from the equation

$$\dot{V}_{O_2}\ \text{ml./min} = 5 \times W\ \text{kg}.$$

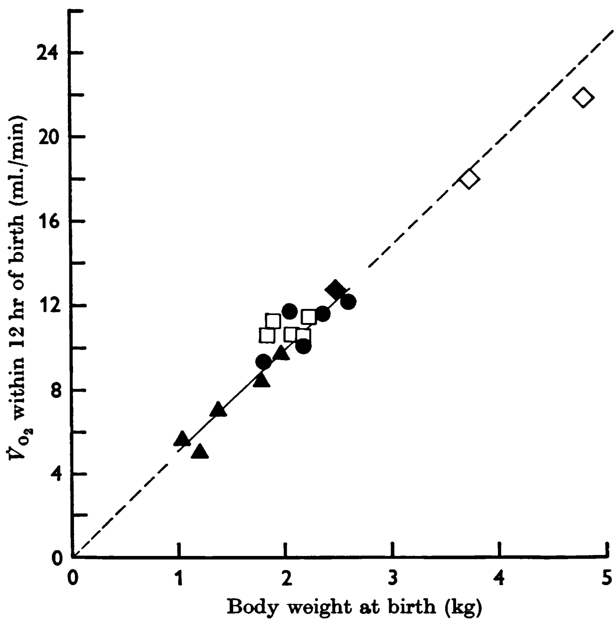

Fig. 3. Ordinates: $\dot{V}_{O_2}$, ml./min, measured within 12 hr of birth. Abscissae: body weight at birth, kg. Symbols and shading as in Fig. 1. The dashed line is defined by $\dot{V}_{O_2}$ ml./min $= 5 \times$ body weight, kg.

It is clear that the points for small-for-dates and large-for-dates babies lie close to the same line, the small-for-dates tending to lie just above it, and the large-for-dates just below it. At birth, therefore, $\dot{V}_{O_2}$ per kg body weight appears to be much the same for undergrown and overgrown babies as it is for normally grown ones.

$\dot{V}_{O_2}$ after birth

All the results of $\dot{V}_{O_2}$ measurements obtained from the nineteen babies are shown plotted against body weight on double logarithmic co-ordinates in Fig. 4. Each group has been given the same symbol as in previous figures, but here shading has been used to indicate age after birth—the

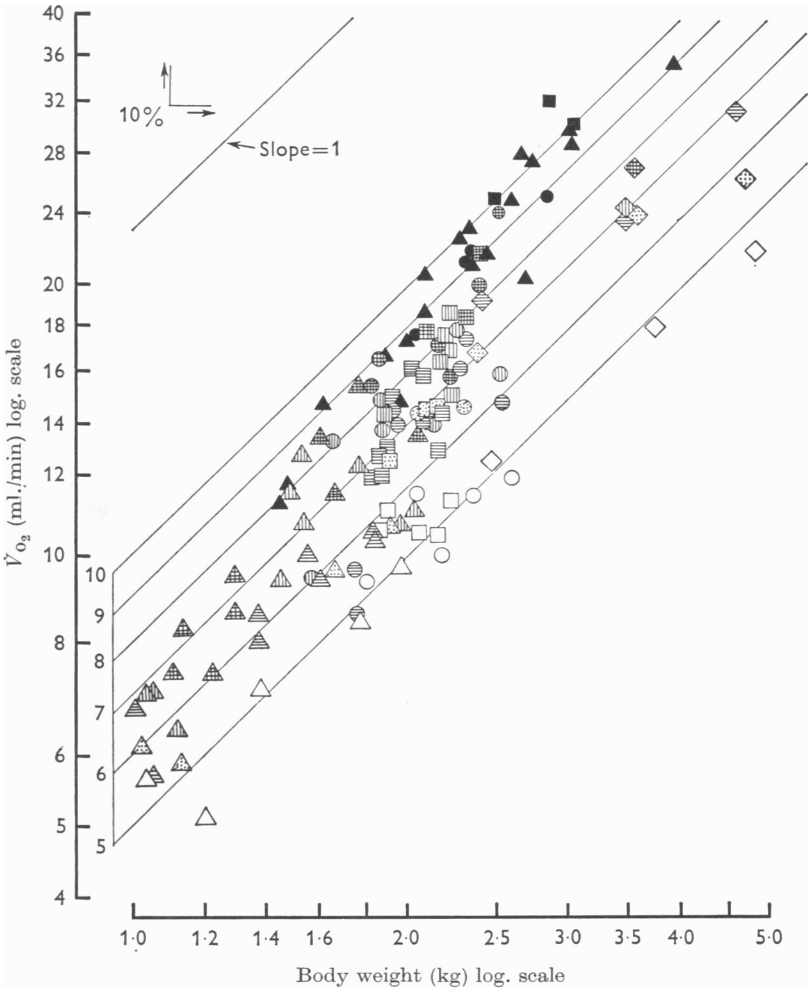

Fig. 4. Ordinates: $\dot{V}_{O_2}$, ml./min; log. scale. Abscissae: body weight, kg; log. scale. This figure shows all the measurements that were obtained from the nineteen babies. Triangles: young pre-term. Circles: pre-term. Squares: small-for-dates. Diamonds: babies of diabetic mothers.

Shading of symbol is a guide to age after birth, the darker the shading, the greater the age; viz.: none: < 12 hr. Stipple: 12–48 hr. Horizontal: 2–7 days. Vertical: 7–14 days. Cross-hatch: 2–4 weeks. Filled: > 4 weeks. Diagonal lines have been drawn as defined by: $\dot{V}_{O_2}$/kg = 5 ml./min, $\dot{V}_{O_2}$/kg = 6 ml./min and etc. Upper left-hand corner: continuous line indicates unit slope: the length of each arm of the right-angle shows the amount of displacement for a 10 % change in each parameter. The points shown here comprise all those shown in Figs. 5–8.

darker the shading, the greater the age (see legend to Fig. 4). It can be seen that the open symbols ($\dot{V}_{O_2}$ at less than 12 hr age) lie, as in Fig. 3, close to the line defined by

$$\dot{V}_{O_2} \text{ ml./min} = 5 \times W \text{ kg.}$$

The points as a whole cover a wide range, and there is a definite tendency for $\dot{V}_{O_2}$ to rise with increasing age as well as with increasing weight. Examination of the changes that take place in an individual baby shows

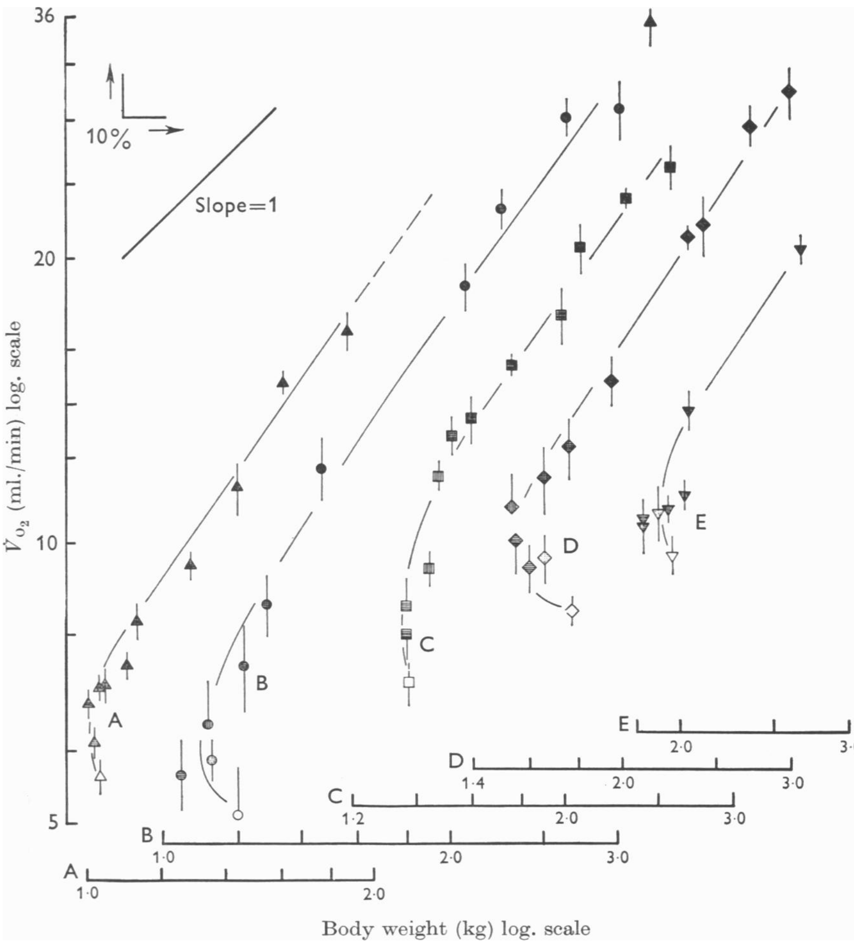

Fig. 5. Young pre-term babies. Ordinates: $\dot{V}_{O_2}$, ml./min; log. scale. Abscissae: body weight, kg; log. scale. Abscissal scales have been staggered to separate the points for different babies, each of whom is represented by a different symbol.

Shading of symbols indicates age after birth as in Fig. 4. Each point represents the mean $\dot{V}_{O_2}$ measured over a period of between 10–30 min, and its associated vertical bar, ± 1 S.D.

that this variation with weight and age is complex. The curves from individual babies are all superimposed in Fig. 4, so in order to see each clearly they are shown again in Figs. 5–8 with the abscissal scales staggered to separate the individual curves (each figure shows a different group). The use of double logarithmic coordinates has the advantage, among others, that comparison between different babies is made easier because, regardless of the value for $\dot{V}_{O_2}$ and body weight, a given percentage change in

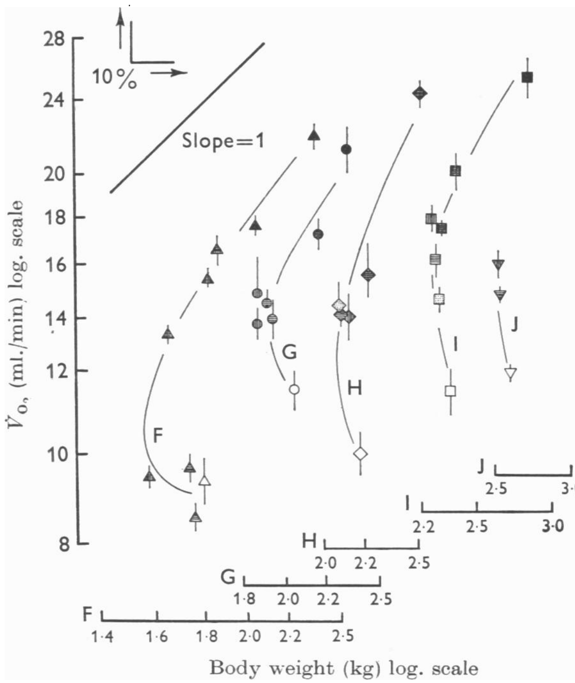

Fig. 6. Pre-term babies. Ordinates, abscissae and other details as for Fig. 5.

either parameter results in a given displacement of a point (see legend to Fig. 4).

The greatest range of values was available from the young pre-term group shown in Fig. 5. Each curve begins by rising almost vertically, with a slight bulge to the left, then settles down to become an approximately straight line. The reason for the initial bulge to the left is that, as is well known, body weight falls for the first few days of life, returning to its initial value at about a fortnight old; but $\dot{V}_{O_2}$ rises continuously with age throughout this period. The linear part of the curve is the region in which weight and age are increasing together. In Figs. 6, 7 and 8 the points could not be expected to cover so wide a range because the babies' stay in hospital was shorter, but the shape of the curves appears similar to what is

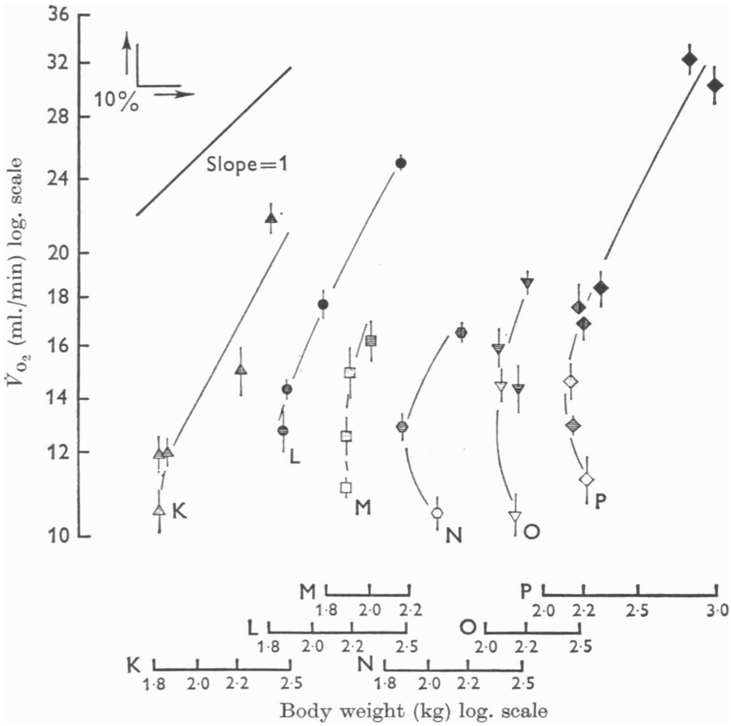

Fig. 7. Small-for-dates babies. Ordinates, abscissae and other details as for Fig. 5.

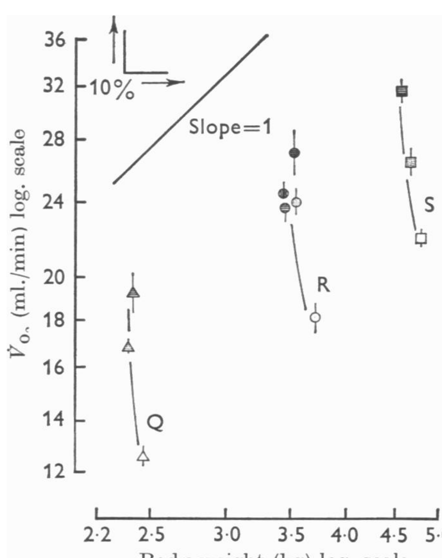

Fig. 8. Babies of diabetic mothers; two are large-for-dates, see text. Ordinates, abscissae and other details as in Fig. 5 except that the abscissal scales did not need to be staggered.

seen in Fig. 5. They all begin with a steep rise and in many cases extend far enough to display a linear region. In all examples the linear region has a slope greater than unity, in fact $\dot{V}_{O_2}$ is rising roughly as (body weight)$^{1 \cdot 3}$. At first sight this may appear to conflict with what was shown in Fig. 3 where the results on new-born babies indicated that $\dot{V}_{O_2}$ was directly proportional to body weight. The difference is that in Fig. 3 all the babies had the same age, while in Figs. 5–8 the differing values of body weight are associated with *different ages*.

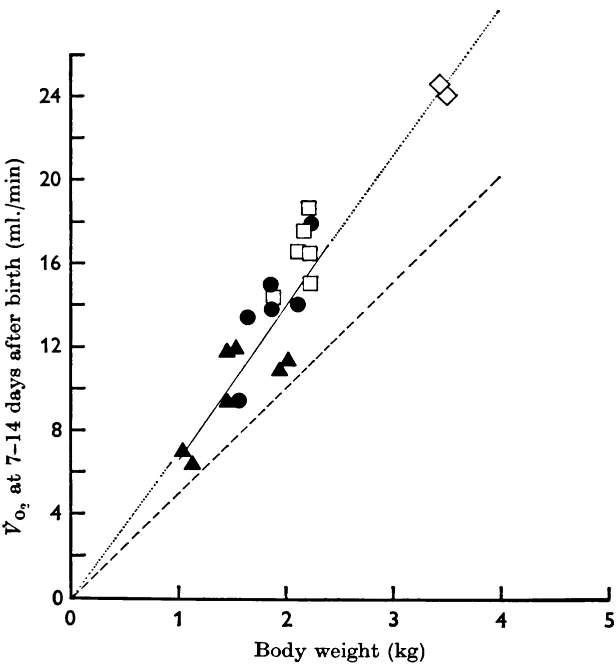

Fig. 9. Ordinates: $\dot{V}_{O_2}$, ml./min, measured at between 7 and 14 days after birth. Abscissae: body weight, kg. Symbols and shading as in Fig. 3, with which this figure is directly comparable. The dotted line is defined by $\dot{V}_{O_2}$ ml./min $= 7 \times$ body weight kg. The dashed line is reproduced from Fig. 3, i.e. $\dot{V}_{O_2}$ ml./min $= 5 \times$ body weight kg.

This illustrates how important it is to remember that $\dot{V}_{O_2}$ is a function of two principal variables, age and body weight. In algebraic terms,

$$\dot{V}_{O_2} = fn \text{ (age, body weight)}$$

Fig. 3 shows that at a constant age, less than 12 hr in this case,

$$\dot{V}_{O_2} = \text{constant} \times \text{body weight}$$

and Fig. 9 demonstrates that at a greater, and again roughly constant, age (7–14 days), the same equation still applies, *but with a different value* *of the constant*. Indeed it appears to a first approximation that all the results can be fitted by the equation

$$\dot{V}_{O_2} = fn' \text{ (age)} \times \text{body weight}.$$

So the problem becomes simplified to finding out what fn' (age) is. Rearranging the equation,

$$fn'\text{(age)} = \dot{V}_{O_2}/\text{body weight}$$

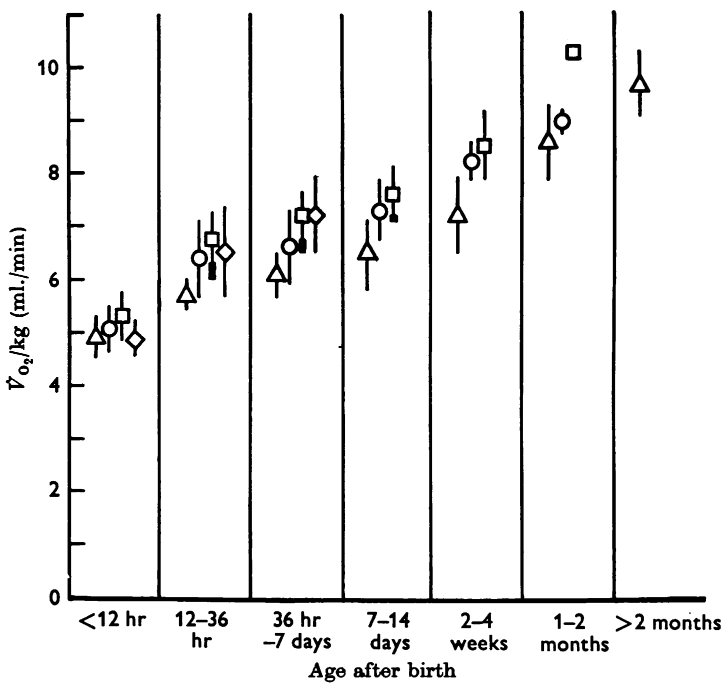

Fig. 10. Ordinates: $\dot{V}_{O_2}$/kg body weight (ml./min). Abscissae: age groups (not to scale). The different symbols indicate different groups, the mean, ±2 S.E. of mean, is shown. Where a filled rectangle is attached to the small-for-dates group, it indicates that the mean differs from that of the young pre-term group at $P < 0{\cdot}05$.

Table 3 and Fig. 10 illustrate how this fraction varies in all four groups. It is evident that $\dot{V}_{O_2}$/kg rises with increasing age in all four groups; however, at all ages, $\dot{V}_{O_2}$/kg of the small-for-date babies is consistently highest, while that of the young pre-term babies is consistently lowest. The differences between these two groups are statistically significant at $P < 0{\cdot}05$ where indicated by the filled rectangles in Fig. 10.

TABLE 3. $\dot{V}_{O_2}$ per kg by group and age class

Values given are: (1) and (2) Mean $\dot{V}_{O_2}$ ml./min kg $\pm$ 1 S.D.; (3) Mean body weight, kg. (4) No. of babies (some babies are not represented in the older age groups). Note that a given infant, when represented within an age group, contributes only one value.

		Age after birth						
			Weight within a few % of birth weight			Weight greater than birth weight		
		< 12 hr	12–48 hr	2–7 days	7–14 days	2–4 weeks	1–2 months	> 2 months
Young pre-term	1	4·93	5·69	6·06	6·48	7·21	8·63	9·70
	2	±0·44	±0·30	±0·50	±0·77	±0·83	±0·77	±0·53
	3	1·47	1·42	1·36	1·42	1·56	2·13	3·12
	4	5	5	5	5	5	5	3
Pre-term	1	5·06	6·40	6·64	7·34	8·25	8·99	—
	2	±0·45	±0·82	±0·78	±0·59	±0·36	±0·12	—
	3	2·19	2·10	2·09	1·96	2·18	2·26	—
	4	5	5	5	4*	4	3	—
Small-for-dates	1	5·31	6·79	7·21	7·63	8·55	[10·09 10·58 individual values for two infants]	—
	2	±0·46	±0·56	±0·52	±0·59	±0·55		
	3	2·00	1·97	2·00	2·15	2·25		
	4	5	5	5	5	3		
Diabetic mother (individual values for $\dot{V}_O$ in birth wt. order)		[5·19 4·87 4·60]	[7·11 6·80 5·70]	[7·98 6·87 6·88]	[7·12]	[7·20]	—	—

* The baby who dropped out of the group at this time was naturally the heaviest one, consequently the mean body weight of those remaining apparently fell.

DISCUSSION

Descriptions of physiological phenomena such as have been given here have two main uses. The first, purely pragmatic and empirical, is to lay down normal standards, so that it is possible to say in a given case whether or not the baby conforms to them. From a clinical standpoint it is particularly important that normal standards should be well established. The second, still largely unattained, is to understand the physiology of the situation and the mechanism behind the changes that take place, since they must have significance for the survival, or at least the well-being, of the baby.

Results of recent investigations agree in broad outline over absolute values and the changes that occur with increasing post-natal age; the differences that arise between different reports appear to concern matters of detail (see e.g. Brück, 1961; Adams, Fujiwara, Spears & Hodgeman, 1964; Levison & Swyer, 1964; Mestyán, Fekete, Bata & Járai, 1964; Adamsons, Gandy & James, 1965; Hill & Rahimtulla, 1965; Scopes

& Ahmed, 1966). In these papers mean values for $\dot{V}_{O_2}$ of babies at birth all fall within the range 4·5–5·2 ml./min.kg, there being no significant difference between premature and full-term infants. Again, there is general agreement that $\dot{V}_{O_2}$ rises soon after birth in both full-term and premature babies, the disagreements if any being concerned with the time course and magnitude of the rise. It would be tedious to examine at length small differences between different studies; for details the papers quoted above should be consulted. In any case, small differences in absolute values may well arise because the type of population sampled and also the experimental techniques and apparatus employed vary between different groups of workers.

Since the same apparatus and experimental technique was used in this study and that of Hill & Rahimtulla (1965) on full-term babies, it is possible to compare the absolute values obtained closely. Over the age range of 0–10 days differences in $\dot{V}_{O_2}$/kg between the four groups of premature babies and the full-term babies are not great, and in general are not significant at the $P = 0{\cdot}05$ level. Values for the small-for-dates babies run consistently about 10% higher than those of full-terms, but this is probably merely a reflexion of the fact small-for-date babies are light in weight largely because they possess a smaller amount of subcutaneous fat (which has a low metabolic rate compared with the rest of the body as a whole) than do other full-term babies. Sinclair & Silverman (1966) and Scopes & Ahmed (1966) both reported a somewhat higher $\dot{V}_{O_2}$/kg in small-for-dates babies than in babies whose weight was within normal limits for gestational age.

At ages greater than two weeks a large and rather surprising difference appears to exist between our results on premature infants and those of others on full-term babies. In the latter $\dot{V}_{O_2}$/kg has been found to stay constant at roughly 7·2 ml./min from two weeks up to one year of age (Benedict & Talbot, 1921; Karlberg, 1952: see Hill & Rahimtulla, 1965, Fig. 8), whereas the metabolic rate of premature infants reported here continued to rise after two weeks, reaching much higher values, around 9 ml./min, by 1–2 months. There seems no obvious explanation for this difference; it suggests, at a purely practical level, that calorie requirements per unit body weight are likely to be considerably greater in premature than in full-term babies after the immediate neonatal period.

The question of what 'metabolic reference standard' is best related to $\dot{V}_{O_2}$ has been investigated by Sinclair, Scopes & Silverman (1967) on a group of babies whose ages covered a much narrower range (2–10 days) than our sample, barely overlapping the third age class in Table 3 and Fig. 10 of this paper. They were concerned to find a function of the body weight that was directly proportional to $\dot{V}_{O_2}$ in order to derive an expression for $\dot{V}_{O_2}$/metabolic reference standard that was constant and thus independent of body weight (range in their sample 1–4 kg). After rejecting body weight itself, surface area, body weight$^{0.73}$, and two more functions of body weight, they concluded that (body weight – extracellular fluid) came closest to the function they were seeking. However, since they had not measured extracellular fluid (ECF) independently on the individual babies, but had calculated it from body weight (see their Table II), in fact they were assessing the constancy of $\dot{V}_{O_2}/(W - 0.561\ W^{0.8025})$.

Unless it has an established theoretical basis, the usefulness of a function should be judged both by its accuracy in predicting values of one variable ($\dot{V}_{O_2}$) from the other (W), and by its simplicity. Sinclair *et al.* (1967) maintain that $\dot{V}_{O_2}/W - \mathrm{ECF}$ is superior to the functions they rejected because the use of these latter 'contributes to a systematic variation in the expression of metabolic rate among neonates'. But a systematic variation that is related to body weight cannot be regarded as an error. In this connexion their Table V gives a false impression because it gives the total standard deviation without breaking it down into its two component parts, the systematic part due to linear regression which is *not an error*, and the residual part (due to deviations from the linearity) which is. The residual error, which is what limits the accuracy of their prediction, does not appear to vary in their Figs. 1–6, nor to be obviously less in the formulation that they have chosen. Over the question of simplicity and ease of calculation there seems little doubt that the equation they favour

$$\dot{V}_{O_2} = (0.16\ W + 11.35)\ (W - 0.561\ W^{0.8025})$$

is unnecessarily complex since their results can be expressed with equal accuracy as a simple power function of body weight,

$$\dot{V}_{O_2} = 5.05 \times W^{1.22} \qquad (r = 0.97,\ P < 0.001),$$

the coefficient of variation of the residual deviation amounting to 5.4 % of the mean. These two equations yield virtually identical values for $\dot{V}_{O_2}$; the line that they define is indicated by the dashed line in Fig. 11 in which the data of Sinclair *et al.* (1967) taken from their Table III have been plotted as $\dot{V}_{O_2}$ against body weight. Since the data are fairly scattered a variety of equations might be found to fit the data reasonably well. An equation which relates $\dot{V}_{O_2}$ to body weight (continuous line in Fig. 11) also fits the data well,

$$\dot{V}_{O_2} = (7.4 \times W) - 2.8 \qquad (r = 0.96,\ P < 0.001)$$

with a coefficient of variance of residual deviation = 14.3 % of the mean. The data do not appear to be fitted quite as well by an equation in which $\dot{V}_{O_2}$ is directly proportional to body weight, see e.g. dotted line in Fig. 11.

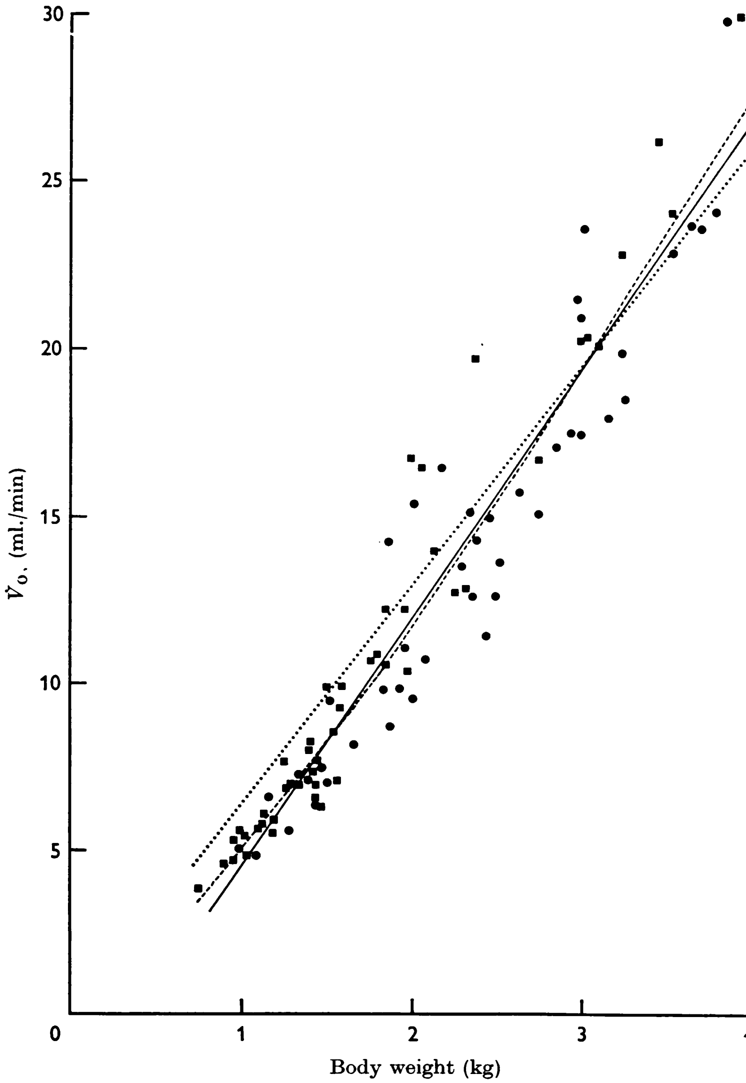

Fig. 11. Data taken from Table III of Sinclair *et al.* (1967). Ordinates: $\dot{V}_{O_2}$, ml./min. Abscissae: body weight (W), kg. ■ American series, ● British series.

Dashed line: regression of log $\dot{V}_{O_2}$ on log W fitted to the data by least squares (92 pairs). Equation $\dot{V}_{O_2} = 5{\cdot}05 \times W^{1{\cdot}22}$ ($r = 0{\cdot}97$, $P < 0{\cdot}001$, coefficient of variance of residual S.D. = 5·4 % of the mean). The dashed line also describes the equation fitted by Sinclair *et al.* (1967) to their data, viz. $\dot{V}_{O_2} = (0{\cdot}16\ W + 11{\cdot}35)\ (W - 0{\cdot}561\ W^{0{\cdot}8025})$.

Continuous line: regression of $\dot{V}_{O_2}$ on W fitted by least squares (92 pairs). Equation $\dot{V}_{O_2} = (7{\cdot}4 \times W) - 2{\cdot}8$ ($r = 0{\cdot}96$, $P < 0{\cdot}001$, coefficient of variance of residual S.D. = 14·3 % of mean).

Dotted line: shows for comparison a line drawn from the equation $\dot{V}_{O_2} = 6{\cdot}5 \times W$.

Clinically it is important to have predictive values, because these decide whether a given individual is abnormal or not; and for this purpose a simple equation (provided its residual variance is reasonably small) is to be preferred. The idea that Sinclair *et al.* (1967) have in mind, that $\dot{V}_{O_2}$ is proportional to $W-$ECF, is interesting, but can be properly tested only by measuring ECF as well as $\dot{V}_{O_2}$ on each individual baby.

We are indebted to the many people on the staff of the London Hospital who co-operated in this study. We wish to thank the consultant Paediatricians and Obstetricians, and the Obstetric Nursing Sisters, particularly Miss Major, for their constant help and interest.

We are particularly grateful to Professor K. W. Cross for continued advice and encouragement, to Dr Kulsum Rahimtulla and Dr Sheila Lewis for performing some of the investigations, and to Mrs Jean Gustavson for her expert assistance.

D.C.R. gratefully acknowledges receipt of a Nuffield Foundation Trainee Paediatrician award. The expenses of part of this work were covered by a grant from the Spastics Society.

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