Foetal growth in the mouse

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In polytocous mammals an inverse relation is known to exist between the number of young in the litter and the size of the young at birth. It has been customary to attribute this to prenatal competition for a limited pool of nutrients in the maternal circulation (Hammond & Marshall 1952).

The present study was undertaken in order to subject the traditional theory to quantitative test. Pregnant mice were killed shortly before term and their foetuses were weighed. Some of the pregnancies had resulted from natural ovulation. Others were obtained by inducing superovulation with hormone treatment, in some cases in adult, and in others in sexually immature females.

Analysis of the foetal weights yielded a number of results at variance with the predictions of the theory of competition, notably the following:

(1) Foetal growth was more affected by the presence of other foetuses if these were in the same, rather than in the opposite, uterine horn.

(2) Foetuses dying in mid-pregnancy, when their nutritional demands would still be small, exerted effects upon the growth of the survivors comparable to those exerted by foetuses surviving the middle period.

(3) The signs of nutritional stress exhibited by sexually immature females carrying abnormally large numbers of foetuses, were not accompanied by a reduction in foetal weight after due allowance for foetal number.

(4) The foetus occupying the top (ovarian) position in the uterine horn was on average significantly lighter than its neighbour.

These results can be better accommodated by an alternative theory of foetal growth (Eckstein, McKeown & Record 1955) which proposes that the chief regulating factor is the pressure at which maternal blood is supplied to the placenta. Some other observations on foetal growth in mice are cited which are also consistent with the haemodynamic theory.

Introduction

It is commonly observed in mammalian species that the size of the young at birth depends on the number of young born. To take an example from a normally monotocous species, the mean birth weight of human twins is about 1 kg (2·2 lb.) less than that of singletons. This comparison is complicated by the tendency of twins to be born prematurely, but even after allowance for the difference in gestation periods, a substantial effect upon birth weight remains. An example of the corresponding effect in a polytocous species, the mouse, is given in figure 1.

The traditional explanation is that there is available for foetal growth only a limited quantity of nutriment in the maternal blood stream: as each foetus draws upon the common pool, less remains to support the growth of the others. An

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inference from this view is that in species with a bicornuate uterus, such as the rabbit or mouse, foetal growth will be retarded by competition from other foetuses to precisely the same extent whether these are present in the same, or in the opposite, horn of the uterus. Hammond & Marshall (1952), generalizing from observations of this type in the rabbit, write: 'The inhibition of growth in the foetuses of large litters, therefore, is not due to the large number present in the uterine horn, but to the limitation of some nutritional substance in the blood supply of the mother as a whole.' In other words, they regard the growth-retarding effects of intra-uterine crowding as arising from systemic and not from local factors.

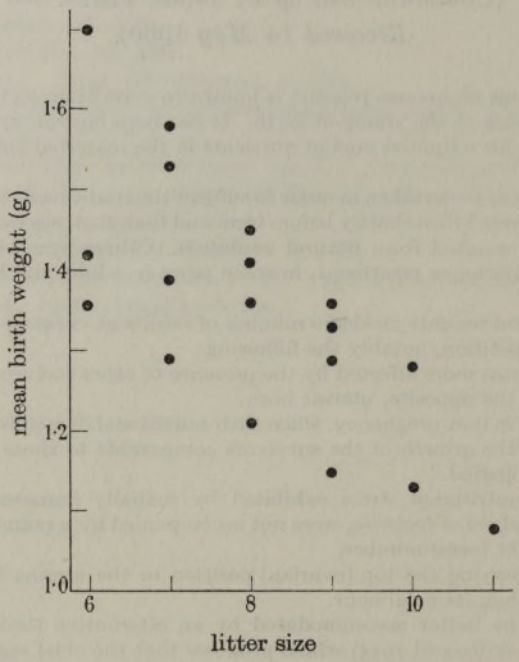

FIGURE 1. Relation between birth weight and litter size derived from eighteen litters of the *TO* random-bred strain of mice.

Recently, however, Eckstein & McKeown (1955) have shown that in the guinea-pig the regulation of foetal growth by litter size is mediated by local as well as by systemic factors. Similarly, Hashima (1956) observed in the course of dissecting seventy-three pregnant mice that where a large discrepancy existed between the numbers of embryos in the two uterine horns 'the average weight in the horn containing the small number tended to be greater than that in the other'.

The present work represents an attempt to compare local and systemic effects in a quantitative fashion and to extend Hashima's observation in other ways. With this object, superovulation and mating was induced in female mice by gonadotrophin treatment (Engle 1927; Fowler & Edwards 1957). The resulting superpregnancies constituted especially favourable material for our purpose in the following respects:

(1) The relative influence on foetal growth of competing foetuses in the same and in the opposite uterine horn could be assessed over a wide range: in the super-

pregnant mouse the number of implants in one horn can vary from 0 up to 16 or more.

(2) The number of embryos dying during early and middle pregnancy is large. It thus becomes feasible to test whether such embryos exert an effect on the size attained by the survivors comparable to that exerted by the other surviving embryos. On the theory of a limited common pool of nutriment, no substantial effect would be expected, since the nutritional demands of such embryos before death must be slight, and after death yet slighter.

(3) Superpregnancy can be induced not only in adult but also in adolescent mice (McLaren & Michie 1959*b*). The latter show signs of severe nutritional strain by the end of pregnancy (McLaren & Michie 1959*c*), so that if systemic supplies of nutriment play an important part, a marked retardation of foetal growth in adolescent superpregnancies might be expected.

Materials and methods

The material used was from the experiment described by McLaren & Michie (1959*b*). Virgin females of the *TO* random-bred strain of mice were injected intraperitoneally with 0·2 i.u. of pregnant mare's serum per 1 g body weight, followed 43 h later by 0·2 i.u. of chorionic gonadotrophin per 1 g body weight. They were then paired with males, and examined the following day (day 0 in our numeration) for vaginal plugs. On day 18 all females were killed and the implants in each uterine horn classified by the criteria of McLaren & Michie (1959*b*) as having survived less than 10 days (early deaths), 10 to 12 days (middle deaths), or more than 12 days (late foetuses). The last category consisted almost entirely of live foetuses. Each live foetus in each horn was weighed to the nearest 0·01 g.

The main series of data was derived from the twenty-four adolescent and twenty-five adult pregnancies containing at least one live foetus in each horn, together with ten pregnancies from spontaneously ovulating adults. A supplementary series from ten treated adults was also analyzed.

Occasional cases of placental fusion between neighbouring foetuses were encountered. This phenomenon occurs more frequently in crowded uterine horns, and also can affect the growth of the foetuses involved (McLaren & Michie 1959*d*). In order to eliminate effects arising from this source, we omitted the weights of such foetuses when calculating mean foetal weights.

The statistical methods used were those of simple and partial regression. The dependent variate in the main series was the mean of the log weights of the foetuses in a horn. These means were not weighted, because of a marked tendency for the intra-horn variance to increase with increasing numbers of foetuses. Hence the amount of information on the mean contributed by a horn containing many foetuses was judged not to differ greatly from the amount contributed by a horn containing few foetuses. In the supplementary series, individual weights of foetuses were not available. Hence the logarithm of the mean was used in place of the mean of the logarithms. The approximation thereby introduced is small.

Separation of local and systemic effects

We assume as a first approximation that the effect of foetal number on log foetal weight is linear. If we do not distinguish between the different types of foetus, then writing y_L for the mean log foetal weight in the left horn of a uterus and x_L, x_R for the numbers of foetuses in the left and right horns, the simplest model states that

$$E(y_L) = \mu_L + \beta_l x_L + \beta_s (x_L + x_R),$$

where E indicates an expected value and β_l and β_s measure the local and systemic effects, respectively. We have a similar equation for the right horn. Adding and subtracting these two equations, we obtain

$$E(y_L + y_R) = \mu_L + \mu_R + (\beta_l + 2\beta_s)(x_L + x_R),$$
$$E(y_L - y_R) = \mu_L - \mu_R + \beta_l (x_L - x_R).$$

TABLE 1. MEAN FOETAL WEIGHTS AND NUMBER OF EMBRYOS IN THE FOUR GROUPS OF MICE

		main series			supplementary series
		treated adolescents	treated adults	untreated adults	treated adults
no. of females		24	25	10	10
mean no. (per female) of	late foetuses (x_1)	13·96	11·32	8·90	14·90
	embryos dying in the middle period (x_2)	3·00	2·12	0·30	1·50
	embryos dying in the early period (x_3)	2·08	6·20	0·30	3·20
mean weight of live foetuses in $10^3 \times$ log decigrams (y)		820·8	886·4	982·2	889·7

Suppose we form the sums and differences of mean log foetal weight and of foetal number for the two horns of each uterus and calculate the simple regressions of sums on sums and of differences on differences, obtaining regression coefficients b_S and b_D; then estimates of β_l and β_s are at once obtained as

$$b_l = b_D,$$
$$b_s = \tfrac{1}{2}(b_S - b_D).$$

The variance of b_l is the same as that of b_D and is estimated in the usual manner. Since the sums and differences are obtained from the same set of uteri, the variance of b_s contains a correlation term (Yates 1939), but calculation showed that the size of this term was negligible in the present data so that we can write

$$\text{var}(b_s) = \tfrac{1}{4}\{\text{var}(b_S) + \text{var}(b_D)\}.$$

This technique is readily extended to allow for the different classes of foetus provided we assume that there is no interaction, i.e. that the effect of the number of foetuses in one class is not influenced by the number in another class. Like the

assumption of linearity, this is probably not strictly true, but our data are not extensive enough to make further complications of the model worth investigating. Under this assumption, the simple regressions on sums and differences are replaced by partial regressions and the values of b_l and b_s for the different classes of foetus are obtained in the same way as before. These values, with their standard errors, are given in tables 2 and 3, the contents of which are more fully discussed in the section headed Results.

TABLE 2. THE LOCAL AND SYSTEMIC EFFECTS ON FOETAL WEIGHT OF NUMBER OF LATE FOETUSES (x_1) AND OF EMBRYOS DYING IN THE MIDDLE (x_2) AND EARLY (x_3) PERIODS OF PREGNANCY

Units are $10^3 \times \log_{10}$

	main series	
	treated adolescents	treated adults
local effect of x_1	$-14{\cdot}24^{**} \pm 2{\cdot}62$	$-8{\cdot}60^{*} \pm 3{\cdot}83$
systemic effect of x_1	$-11{\cdot}11^{*} \pm 3{\cdot}96$	$-7{\cdot}70^{*} \pm 3{\cdot}76$
local effect of x_2	$-5{\cdot}68 \pm 3{\cdot}46$	$-10{\cdot}31 \pm 5{\cdot}26$
systemic effect of x_2	$-9{\cdot}00^{*} \pm 4{\cdot}16$	$-4{\cdot}31 \pm 9{\cdot}32$
local effect of x_3	$+0{\cdot}39 \pm 4{\cdot}38$	$-5{\cdot}18 \pm 2{\cdot}90$
systemic effect of x_3	$+1{\cdot}84 \pm 6{\cdot}74$	$-2{\cdot}26 \pm 3{\cdot}82$

$^{*}\ P < 0{\cdot}05$ $^{**}\ P < 0{\cdot}01$

TABLE 3. RECALCULATION OF THE LOCAL AND SYSTEMIC EFFECTS ON FOETAL WEIGHT AFTER DISCARDING x_3 FROM THE ANALYSIS (*see* TABLE 2). THE UNTREATED ADULTS AND THE SUPPLEMENTARY SERIES OF TREATED ADULTS HAVE BEEN INCLUDED

Units are $10^3 \times \log_{10}$

	main series			supplementary series
	treated adolescents	treated adults	untreated adults	treated adults
local effect of x_1	$-14{\cdot}20^{**} \pm 2{\cdot}53$	$-8{\cdot}25^{*} \pm 4{\cdot}01$	$-10{\cdot}73^{**} \pm 2{\cdot}84$	$-10{\cdot}74^{**} \pm 2{\cdot}78$
systemic effect of x_1	$-11{\cdot}31^{**} \pm 3{\cdot}85$	$-6{\cdot}44 \pm 3{\cdot}69$	$+2{\cdot}34 \pm 6{\cdot}70$	$-10{\cdot}72^{*} \pm 3{\cdot}67$
local effect of x_2	$-5{\cdot}67 \pm 3{\cdot}37$	$-10{\cdot}71 \pm 5{\cdot}51$	—	—
systemic effect of x_2	$-9{\cdot}45^{*} \pm 3{\cdot}82$	$-2{\cdot}18 \pm 8{\cdot}19$	—	—

$^{*}\ P < 0{\cdot}05.$ $^{**}\ P < 0{\cdot}01.$

Comparisons between series

It is of interest to compare the effects of the x-variables on foetal weight in the different series. If it is found that these effects, as measured by the regression coefficients, do not differ significantly we may ask further whether the regression planes may be regarded as coinciding so that any difference in mean foetal weight between two series may be accounted for by the difference in mean foetal number. Regressions of total or mean foetal weight on total foetal number are appropriate for this purpose; in fact, the sum of the mean log foetal weights in the two horns

has been used as dependent variate. The results of this type of analysis are conveniently presented in the form of an analysis of variance in which mean squares measuring departures from coincidence and parallelism are compared with a residual mean square. Such analyses are given in table 4, the content of which is more fully discussed in the following section.

TABLE 4. TESTS OF PARALLELISM AND COINCIDENCE OF REGRESSIONS APPLIED TO THE MAIN BODY OF DATA: REGRESSIONS OF y ON x_1 AND x_2 (SUMS OF LEFT AND RIGHT HORNS)

A. Treated adults vs. treated adolescents

variation due to	d.f.	m.s.
lack of coincidence	1	30733
lack of parallelism	2	22336
residual	43	16607

B. Treated adults vs. control adults

variation due to	d.f.	m.s.
lack of coincidence	1	65937
lack of parallelism (regression on x_1 only)	1	11318
residual	30	18078

Neither in comparison A nor in comparison B do the mean squares for lack of coincidence and lack of parallelism reach significance at the 5% level.

RESULTS

The 49 treated females in the main series which carried at least one live foetus in each horn yielded 98 uterine horns for analysis. These contained a total of 556 live foetuses, which ranged in weight from 0·31 g up to 1·30 g. The number of implants varied from 1 up to 16 per horn, and from 5 up to 32 per pregnant female. The mean foetal weights for the 98 horns ranged from 0·47 g up to 1·16 g.

A very large part of the variation in foetal weights was plainly due to the variation in the number of foetuses in the horn. This is shown in figure 2, where mean foetal weight is plotted against the number of late foetuses in the horn. This representation does not, of course, distinguish between local and systemic effects. The fact, however, that substantial local effects exist is immediately revealed when the right–left differences in foetal weight are plotted against the right–left differences in foetal number, as in figure 3. These graphic representations make no allowance for possible effects (whether local or systemic) of embryos failing to survive into the late period, nor do they permit the separate assessment of any systemic effects which may exist. In order to elucidate these questions a regression analysis, along the lines outlined in the last section, was undertaken. Such an analysis is also necessary for deciding whether there are real differences in foetal growth as between the various groups of mice, after making allowance for effects of foetal number.

The mean weights of live foetuses in the various groups are given in table 1, together with the mean numbers of late foetuses and of embryos dying in the middle and early periods of pregnancy.

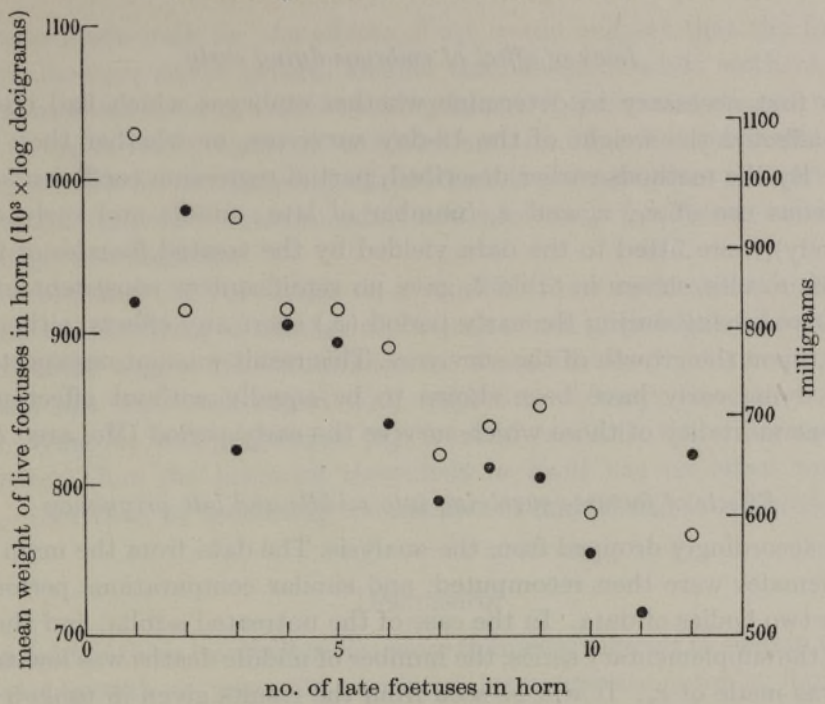

FIGURE 2. Relation between 18-day mean foetal weight and the number of late foetuses in the uterine horn in superpregnancies induced in adolescent (●) and adult (○) female mice of the *TO* strain. The apparent tendency for the adolescent mothers to have smaller foetuses than the adults disappeared after allowance was made for the effect of foetuses dying in mid-pregnancy, which are more numerous in adolescent than in adult superpregnancies.

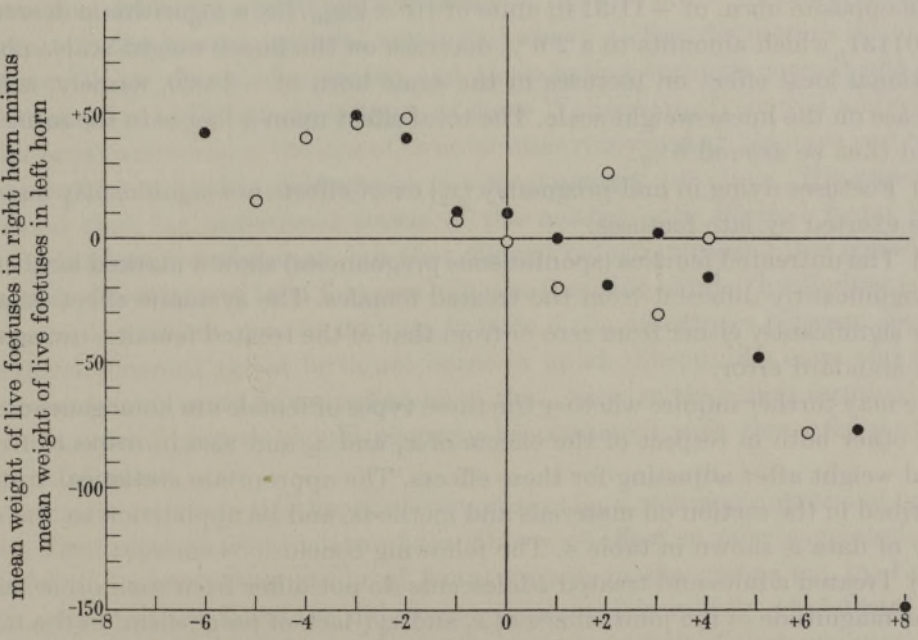

FIGURE 3. The local effect of foetal number upon foetal weight. The more crowded horn tends to contain lighter foetuses than the less crowded horn. ●, adolescent; ○, adult.

Lack of effect of embryos dying early

It was first necessary to determine whether embryos which had died before 10 days affected the weight of the 18-day survivors, or whether they could be ignored. By the methods earlier described, partial regression coefficients, making simultaneous use of x_1, x_2 and x_3 (number of late, middle and early embryos, respectively), were fitted to the data yielded by the treated females of the main series. The results, shown in table 2, gave no significant or consistent indication that embryos dying during the early period (x_3) exert any effects, either local or systemic, upon the growth of the survivors. This result was not unexpected, since embryos dying early have been shown to be equally without effect upon the subsequent mortality of those which survive the early period (McLaren & Michie 1959*b*).

Effects of foetuses surviving into middle and late pregnancy

x_3 was accordingly dropped from the analysis. The data from the main series of treated females were then recomputed, and similar computations performed for the other two bodies of data. In the case of the untreated adults, and the treated adults of the supplementary series, the number of middle deaths was low and hence no use was made of x_2. It will be seen from the results given in table 3 that the standard errors of the regression coefficients are rather large, but the following main conclusions may be drawn.

(1) Both local and systemic effects upon growth exist and are of comparable magnitude. Taking the treated adolescents as an illustration, each additional late foetus exerted an effect on the growth of every other foetus, whether in the same or the opposite horn, of $-11{\cdot}31$ in units of $10^3 \times \log_{10}$, i.e. a logarithmic decrement of 0·01131, which amounts to a 2·6 % decrease on the linear weight scale; plus an additional local effect on foetuses in the same horn of $-14{\cdot}20$, namely, a 3·3 % decrease on the linear weight scale. The total effect upon a foetus in the same horn would thus be around 6 %.

(2) Foetuses dying in mid-pregnancy (x_2) exert effects not significantly less than those exerted by late foetuses.

(3) The untreated females (spontaneous pregnancies) show a marked local effect, not significantly different from the treated females. The systemic effect does not differ significantly either from zero or from that of the treated females, owing to its large standard error.

We may further inquire whether the three types of female are homogeneous with each other both in respect of the effects of x_1 and x_2 and also in respect of mean foetal weight after adjusting for these effects. The appropriate statistical test was described in the section on materials and methods, and its application to the main body of data is shown in table 4. The following conclusions emerge:

(1) Treated adults and treated adolescents do not differ from each other, either in the magnitude of the joint effects of x_1 and x_2 ('lack of parallelism' in the table), or in mean foetal weight after allowance for these effects ('lack of coincidence'). This last point is relevant to the hypothetical role of nutritional stress which was mentioned in the Introduction. A superficial examination of figure 2, in which

allowance is made only for the effects of x_1, would suggest that the foetuses of adolescent mothers are in general smaller than those of adult mothers. The full analysis shows this to be an artifact arising from the presence of a larger number of foetuses dying in mid-pregnancy in adolescent than in adult pregnancies. When allowance is made for the retarding effect which these exert upon the growth of the survivors, the difference between adult and adolescent females as culture media for foetal growth vanishes.

(2) Treated and control adults do not differ from each other, either in the magnitude of the effects of number of foetuses ('lack of parallelism' in table 4) or in mean foetal weight after allowance for these effects ('lack of coincidence'); parallelism has here been tested with respect to x_1 only, since the number of foetuses dying in mid-pregnancy (x_2) is very small in the untreated control pregnancies. Thus the hormone treatment in itself has no effect upon foetal growth, other than by increasing the number of middle and late foetuses.

Discussion

In the light of these results it seems more than ever difficult to sustain the theory that foetal growth is primarily regulated by competition for a limited total amount of circulating nutriment. Such a mechanism may perhaps come into play under conditions of nutritional extremity, as when human birth weights fall in conditions of near-starvation (see Millis 1953 for references). But the results obtained from our material suggest that this mechanism played at most a minor role, in spite of the fact that superpregnancy induced in the adolescent female constitutes in itself a nutritional extremity of the first order. It is worth pointing out that in the human material mentioned above a clear distinction is not made between direct effects of nutrition and those acting through curtailment of the gestation period. On the other hand, in sheep Wallace (1948) showed a clear effect of maternal nutrition on the size of twin foetuses recovered at 144 days *post coitum*. The gestation period in this species is approximately 148 days. His experiment revealed that the nutritional status of the mother only affected foetal growth during the last 6 weeks or so, but that dietary reduction during this period could diminish the weight of twin foetuses by more than one-third. This finding is easier to reconcile with the present findings in mice if the differences between species in the developmental age at birth are borne in mind. Sheep, like cows and horses, are considerably more advanced at birth than mice, so that their terminal phase of intra-uterine growth should properly be compared with the early post-natal growth of mice.

As an alternative to the theory of competition for a common nutritional pool, we may consider an interpretation of the litter-size effect in mice suggested by the careful and illuminating study of foetal growth in the guinea-pig by Eckstein *et al.* (1955). They found, as did Hammond (1935) in rabbits, that foetal size is positively correlated with placental size; and they showed that placental size is affected by the number of implants through both local and systemic channels of influence. They also showed that foetal size is affected by foetal number—locally

and systemically—even after allowing for effects of placental size. Eckstein *et al.* (1955) suggest that this latter phenomenon—the local and systemic effects of foetal number upon foetal size, irrespective of placental size—is due to limitation of blood supply to the uterus. We may perhaps go further, and seek to relate the entire nexus of cause and effect, depicted by us graphically in figure 4, to a single prime cause. If it is conceded (1) that the growth of the foetus is dependent on the quantity of nutrients taken up from the maternal blood circulating through the placenta, (2) that this in turn depends both upon the size of the placenta and upon the pressure at which maternal blood reaches the placenta, and (3) that the growth of the placenta itself is also dependent on the amount of blood reaching it, then

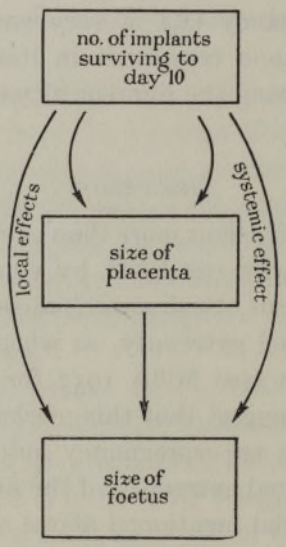

FIGURE 4. Pathways of influence leading from embryonic number at day 10 to the size attained by foetuses surviving to term.

the problem reduces to one of hydrodynamics. In that event all local and systemic effects of implant number upon foetal size, whether exerted directly or via placental size (see figure 4), could be related to the pressure at which maternal blood is delivered to each implantation site down the corresponding offshoot of the uterine artery.

Figure 5 shows a schematic representation of the uterine vasculature of the mouse. Since the resistance to blood flow through the placenta is rather low, the greater the number of offshoots draining one of the two main loop vessels the less will be the pressure within any one of them. This fact is sufficient, on the assumptions listed above, to account for the local effect upon foetal and placental growth, and Eckstein *et al.* argue that it may also account for the systemic effect, since 'reduction of pressure in one uterine artery is likely to be transmitted in part to the other'. The systemic effect can hardly be attributed to competition for a limited nutritional pool, since our data have shown that foetuses dying in mid-pregnancy can still exert a substantial systemic effect (table 3). Whether or not a haemodynamic explanation for the systemic effect is justified, the local effect

is worth examining further from this point of view, as there exist published observations bearing directly upon it.

The first point to be considered is the local effect of foetuses dying in the middle period. Since the death of a foetus presumably terminates the flow of blood through its placenta, one might expect its effect upon the growth of the survivors also to be terminated. This would, however, be to ignore the fact that when a foetus survives into the period of placentation, the vascular supply gained by its placenta could limit the size attained by other placentas in the same horn, and hence the growth of the surviving foetuses. One would expect, therefore, that a foetus dying in the middle period should exert a local effect, although a somewhat smaller one than

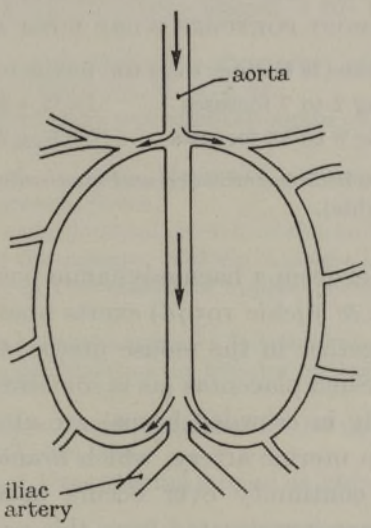

FIGURE 5. Schematic representation of blood flow through the uterine vasculature of the mouse. In the simplest case each hypertrophied offshoot of the main loop vessel supplies one embryo.

that exerted by a late foetus, and our data are consistent with this expectation. Since, according to Eckstein *et al.*, there is a systemic effect upon placental size, the otherwise puzzling fact that middle deaths can exert a systemic effect finds a ready explanation: although such foetuses barely survive their own placentation, they do thereby survive long enough to influence mean placental size (and hence mean foetal size) in the opposite horn.

The next points to consider concern refinements of the haemodynamic principles outlined in figure 5. In a system of side-branches from a loop vessel which is fed at either end, as in the vascular system illustrated, a pressure gradient must be encountered moving from either end towards the middle. According to the data of McLaren & Michie (1959*a*), this is paralleled by the distribution of foetal weights, which form a U-curve from the ovarian to the vaginal end of the uterine horn.

The only irregularity concerns the topmost foetus of all, which departs abruptly from the U-curve, being significantly *lighter* than its neighbour. This exception, however, supports rather than undermines the haemodynamic generalization: in the crowded horns the top foetus frequently shares a single offshoot with the ovary,

as indicated by the bifurcating branch at the top left of figure 5, and hence must be expected to receive a diminished blood supply; and it is precisely in the crowded horns (eight or more foetuses) in our material that we find the restriction of growth of the top foetus to be concentrated. Table 5 shows an analysis of the main series of pregnancies described in the present paper, which yielded 61 uterine horns in which both the upper two implantation sites were represented by live foetuses, together with 19 uterine horns derived from an unpublished series of induced superpregnancies. The two bodies of data were in good agreement and have been combined.

TABLE 5. COMPARISON BETWEEN TOP AND SECOND FOETUS IN HORNS WHERE THE TWO UPPERMOST FOETUSES WERE BOTH ALIVE AT DAY 18

	second foetus is heavier than top foetus by	
in horns containing 2 to 7 foetuses	$1{\cdot}6\,\% \pm 2{\cdot}2\,\%$	$n = 41$
in horns containing 8 to 13 foetuses	$10{\cdot}3\,\% \pm 2{\cdot}7\,\%$	$n = 39$

Significance of the difference between crowded and uncrowded horns: $t_{(78)} = 2{\cdot}39$, $P < 0{\cdot}02$ (based on analysis of log weights).

Finally, we must consider from a haemodynamic point of view the effect which placental fusion (McLaren & Michie 1959*d*) exerts upon foetal growth. When two embryos implant close together in the mouse uterus, the neighbouring placentas sometimes fuse together. Such placentas (as is sometimes the case with non-fused close neighbours, especially in crowded horns) are almost always supplied by a single offshoot of the main uterine artery, which branches as it nears the uterine horn. Whether vascular continuity ever occurs between the two foetuses is unknown. In the single case investigated from this point of view by McLaren & Michie, there proved to be no evidence of vascular continuity between the fused partners; and it seems likely that the mouse differs in this respect from the cow, in which blood exchange between conjoined twin foetuses is the rule.

Each member of a pair of fused placentas tends to be noticeably smaller than other placentas in the same horn, and on the argument developed above we might expect to find a consequent retardation of foetal growth also. This proves to be so. Where both members of a conjoined pair of foetuses were alive on day 18, their mean weight was found to be about 17 % less than that of their non-fused siblings in the same horn (McLaren & Michie 1959*d*). However, when one member of the pair was dead, the survivor showed no retardation of growth relative to the other live foetuses in the horn. This again might be expected on haemodynamic grounds. After the death of one foetus, and the consequent degenerative changes in its placenta, the blood flowing down the single offshoot of the uterine artery which supplies the pair will be shunted to the surviving foetus. This increased blood supply will tend to compensate for the handicap of reduced placental size.

It is, of course, unlikely in the extreme that the haemodynamic theory will prove adequate to embrace all known effects on foetal growth. But even the limited range of effects described in the present study seems to overtax the resources of the traditional theory.

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