the fourth month the uterine wall has been reduced to one-third of its original (non-pregnant) thickness. In the last month there is an insignificant increase in thickness. This is caused solely by the high figures obtained at the 147th day, and resulting from the general oedematous condition of all the genitalia at this stage.

Discussion. The small, pale and contracted uterus of the non-pregnant ewe undergoes many changes during pregnancy. By the eighteenth day the horns appear slightly puffy and by its slightly larger size it is possible to distinguish the horn in which the ovum has become implanted. At about this time the colour of the organ changes to a distinct pink and numerous very tortuous subserous bloodvessels become visible. As gestation progresses so these vessels become larger and less tortuous, the colour becomes redder, and the size-difference between the horns becomes much more distinct. After the 38th day/there is also a change in the shape of the horns, this being the result of more rapid growth along the greater curvatures. Seven days later the uterine wall has a bluish-grey colour and the subserous vessels are large and pursue an almost straight course. The largest are to be found along the lesser curvatures, and from these branches run across the uterine horns at right angles to their long axes. By this time the walls have become markedly thinner and through them the outlines of the cotyledons may be distinguished. From the middle of gestation the pregnant horn grows much more rapidly than its fellow and the discrepancy in size becomes so marked that towards the end of the fourth month the non-gravid horn has become merely an appendage of the other. At this stage the walls have become very thin and vascularity is pronounced throughout the organ. This state is maintained until the approach of parturition. At the 147th day the thickness of the wall is increased as a result of a general oedema of the genitalia.

In the non-pregnant uterus the mucosa is pale and but slightly moist. Early in pregnancy there is a slight reddening at the site of implantation and this spreads repidly until at the 45th day the entire mucosa is markedly vascular. At this stage the epithelial

TABLE 17. NUMBER OF COTYLEDONS.

Groups of Ewes No	Class	No. of Ewes.	Mean number of Cotyledons. Pregnant side	Non-preg. side	Total Groups	Significance Tests. W. Gr. 1.	W. Preced. Gr.
1.	Non-preg	11	46.64	45.26	46.00		
2.	1st Month	12	44.17	42.92	43.54	-	-
3.	2nd "	8	42.13	37.63	39.38	X X	X
4.	3rd "	6	43.83	39.33	41.58	X	-
5.	4th "	7	37.71	36.57	37.14	X X	X
6.	5th "	5	43.00	40.80	41.90	-	X
Average			43.31	41.02			

Facing page 61.

lining appears to have been destroyed (at least the surface is not smooth and clear) and the surface is covered with a layer of dirty greyish sticky material. As a result of this the allanto-chorion is found to adhere to the inner surface of the uterine wall and in stripping it off care has to be exercised not to rupture the sac. This condition persists until midway through the fourth month, after which the epithelial lining appears to be restored and with the disappearance of the slimy coating the mucosa is again smooth, fairly moist and of a light red colour. At this stage the amount of adherence between the uterus and the foetal sac is negligible.

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4. PLACENTA.

It has been seen (Table 14 & Fig.12) that the weight of the placenta increases to a peak in the third month, after which it drops fairly rapidly. In an attempt to determine the cause of this behaviour the numbers and the sizes of the cotyledons have been studied. Details of the former are presented in Table 17 & Fig.15.

When these data are analysed in the manner described in connection with the thickness of the uterine wall, it is found that there is a significant difference between the pregnant and non-pregnant sides of the uterus. The excess in favour of the former side is never great and falls far short of the figure (50%) mentioned by Bergmann (1922) in his work on the bovine. From the tests it appears that there are significant differences at the various stages of pregnancy. Here it must be remembered that in the first two groups it was impossible to distinguish between functional and non-functional cotyledons, thus the figures given represent counts of all the cotyledons,as compared with counts only of functional cotyledons in the remaining groups. Hence it is not surprising to find that the numbers for the first two groups are higher than those of any other group. As this method of testing is open to criticism, it is more satisfactory to employ group No.3.(the first in which functional cotyledons are easily recognizable) as the standard for

TABLE 18. DIAMETER OF COTYLEDONS.

Groups of Ewes. No	Class	No. of Ewes.	Mean Diameter of Cotyledons. Preg. Side	Non-preg. Side	Total Groups.	Significance Tests. W.Gr.1.	W. Preced. Gr.
1	Non-preg	11	.28cm	.30cm	.28cm		
2.	1st Month	12	.42cm	.39cm	.40cm	-	-
3.	2nd "	8	1.86cm	1.47cm	1.67cm	X X	X X
4.	3rd "	6	3.45cm	3.24cm	3.35cm	X X	X X
5.	4th "	7	3.04cm	2.94cm	2.99cm	X X	X
6.	5th "	5	3.00cm	3.00cm	3.00cm	X X	-
	Average		1.63cm	1.52cm			

TABLE 19. HEIGHT OF COTYLEDONS.

Groups of Ewes. No	Class	No. of Ewes.	Mean Height of Cotyledons Preg. Side	Non-preg. Side	Total Groups	Significance Tests. W.Gr.1.	W. Preced. Gr.
1	Non-preg	11	.15cm	.16cm	.16cm		
2	1st Month	12	.16cm	.15cm	.15cm	-	-
3	2nd "	8	.63cm	.55cm	.59cm	X X	X X
4	3rd "	6	1.42cm	1.37cm	1.39cm	X X	X X
5	4th "	7	1.50cm	1.46cm	1.48cm	X X	-
6	5th "	5	1.16cm	1.16cm	1.16cm	X X	X X
	Average		.681cm	.656cm			

Facing page 62.

comparison. When this is done it appears that, in spite of a fair degree of variation in the last four groups, none of the differences are significant. Therefore, the differences observed may be ascribed to "unfair" counts in the first two groups, and it may be concluded that, whatever the true position regarding functional cotyledons in the first month (in Group 1 their number is nil) the observed variations in the weight of the placenta are not caused by variations in the numbers of cotyledons.

As a result of the above conclusion, it becomes necessary to consider the size of the cotyledons at the various stages of pregnancy. For this purpose two dimensions (diameter & height) have been studied. In each instance the average of the readings for the largest cotyledon in the horn and one representing the modal size of that horn, is employed. Details of these representative figures are presented in Tables 18 & 19 and Figs. 16 & 17. Both these dimensions increase rapidly (becoming significant in the second month) up to the end of the third month. After this their behaviour differs, the diameter dropping significantly in the fourth month and then maintaining its level in the fifth, whereas the height still increases (although insignificantly) in the fourth month and then undergoes a significant decrease in the last month of pregnancy. However, by the end of gestation both dimensions are significantly lower than they were in the third month. It is clear that the placental weight is affected mainly by this change in the size of each individual cotyledon.

<u>Discussion.</u> It has been seen that during pregnancy the cotyledons increase enormously both in diameter and in height. Apart from this enlargement there are other changes which may be observed macroscopically. In the non-pregnant uterus the cotyledons appear to be arranged in four longitudinal rows. All are of the same size and are just visible as pinhead-sized, brownish centres with pale narrow peripheral zones. In dioestrum they are level with the surface of the mucosa, but during oestrum they become slightly swollen and elevated. Early in pregnancy a change is evident ~~and~~

Facing P. 63.

PLATE NO. 3. UTERUS OF EWE
69 DAYS PREGNANT
LAID OPEN TO SHOW
SIZE AND DISTRIBUTION
OF COTYLEDONS.
Pregnant horn on the
right & body below.

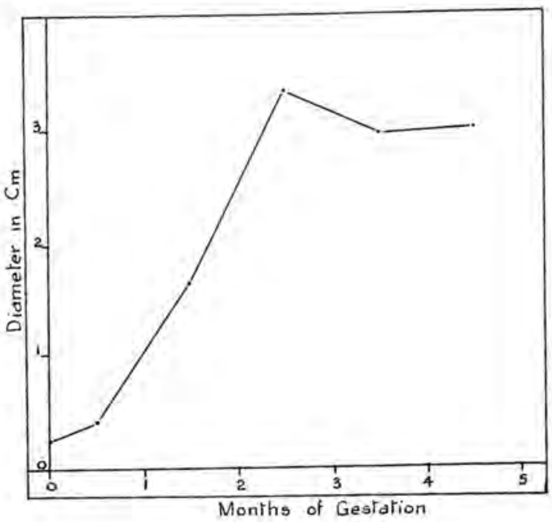

FIG. 16. DIAMETER OF COTYLEDONS.

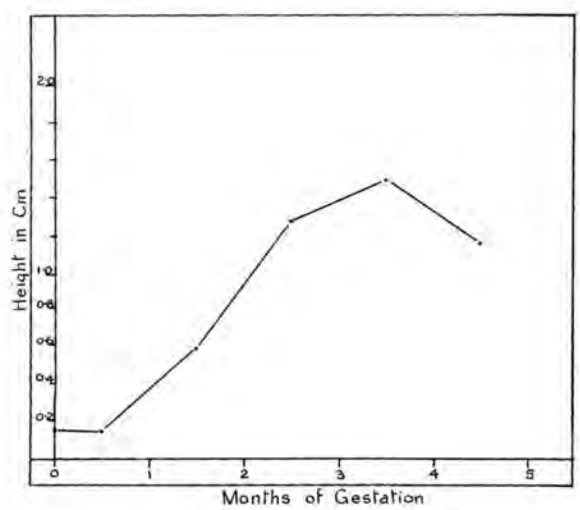

FIG. 17. HEIGHT OF COTYLEDONS.

and by the 21st day both the size of the central portion and the elevation of the cotyledon are visibly increased. During the next few days the brownish centre, previously concave, becomes flat and numerous pin-point red spots appear all over its surface. On the 27th day the cotyledon has the form of a small nodule under the epithelial layer of the uterus. Four days later the central portion has a distinct red colour and a pitted appearance, while the periphery has become elevated to form a thin circular lip around the wide flat centre. From this time until the 80th day the cotyledon develops rapidly: it enlarges and the peripheral lip begins to curl inward, thus decreasing the size of the central cup and trapping the foetal cotyledon which has come to rest upon the surface of the cup. At the same time the base of the cotyledon becomes convex and detaches itself from the surrounding tissue to such an extent that finally the entire cotyledon is attached to the uterine wall merely by a thin mucosal penduncle.

At about the end of the third month the cotyledons appear to have reached their maximum development. The cups are small and the rolled-in edges resemble motor-tyres in miniature. In some instances the cups tend to lose their circular shape and become elongated slits. From this stage onward fairly large blood clots of long standing are visible in the cups of the cotyledons. Apart from a tendency to decrease somewhat in size (partly due to a tighter rolling in of the edges) the cotyledons do not undergo further change until about the 140th day, after which the turned-in periphery relaxes and the whole cotyledon opens out flat, with the central portion partially everted and covered with clotted blood. By the 147th day, most of the cotyledons resemble flattened reddish-black discs, while in a few the eversion has been so marked as to give the appearance of a mushroom (similar to the convex cotyledons of the bovine.) At this stage the attachment of the membranes is not firm and they may be pulled away with ease. Usually the entire central portion of the cotyledon comes away, leaving an empty thin-walled cup.

In the above description only the general appearance of the

TABLE 20. LENGTH OF FALLOPIAN TUBES.

Groups of Ewes No.	Class	No. of Ewes.	Mean Length in Cm. Preg. Side.	Non-preg. Side	Total Groups	Significance Tests. W.Gr.1.	W. Preced.Gr.
1	Non-preg	11	15.41	15.05	15.23		
2	1st Month	12	15.55	15.88	15.72	-	-
3	2nd "	8	18.00	17.13	17.56	X X	X X
4	3rd "	6	17.17	17.08	17.13	X	-
5	4th "	7	17.64	17.57	17.61	X X	-
6	5th "	5	18.60	17.90	18.25	X X	-
	Average		16.73	16.35			

TABLE 21. DIAMETER OF FALLOPIAN TUBES.

Groups of Ewes No.	Class	No. of Ewes.	Mean Diameter in Cm. Preg. Side	Non-preg. Side	Total Groups	Significance Tests. W. Gr.1.	W. Preced.Gr.
1	Non-preg	11	.21	.21	.21		
2	1st Month	12	.19	.20	.20	-	-
3	2nd "	8	.19	.19	.19	-	-
4	3rd "	6	.19	.19	.19	-	-
5	4th "	7	.19	.19	.19	-	-
6	5th "	5	.20	.20	.20	-	-
	Average		.196	.196			

Facing page 64.

cotyledons at each stage has been mentioned. However, at one and the same time a variety of phases of developement may be encountered. This is well illustrated in the accompanying plate (No.3.) Development is initiated at the site of implantation and throughout the progressive stage the largest and best developed cotyledons are to be found here. In the opposite horn growth is slower and the maximum is reached later. In both horns the largest cotyledons are found towards the centre, while the size decreases towards the apices and towards the body. In the latter only a few cotyledons are present and these are but poorly developed. During the last two months there is practically no difference between the cotyledons of the pregnant and non-pregnant horns, although the differences at different situations in the horn persist until parturition. The smaller cotyledons, although slower in growth, appear to reach the same stage of differentiation as the largest ones.

The foetal part of the placenta also develops fairly early. At the 21st day of pregnancy dull white areas appear on the allanto-chorion wherever it touches the surfaces of the maternal cotyledons. A few days later these patches have become almost opaque and at the 31st day numerous closely grouped pin-point red spots ~~on these areas~~ mark out on these areas the size and shape of the central portions of the maternal cotyledons. At this time there is a very loose attachment of membrane to cotyledon. The red spots increase in size and coalesce and small vessels can be distinguished running from these circumscribed areas to the umbilical cord. By the 45th day these areas have developed into thick discs firmly attached to the outer surface of the allanto-chorion. By this time there is a fair degree of adherence between the discs and the maternal cotyledons. From now on the edges of the latter curl inward to hold the foetal cotyledons firmly in position, thus completing the cotyledonary attachment.

5. FALLOPIAN TUBES.

The tubes were considered from the point of view of length, ~~of~~ diameter and weight. For each of these characteristics an analysis similar to that described in connection with the thickness

TABLE 22. WEIGHT OF FALLOPIAN TUBES.

Groups of Ewes. No.	Class.	No. of Ewes	Mean Weight in Gm. Preg. Side.	Non-preg. Side	Total Groups.	Significance Tests. W.Gr.1.	W. Preced.Gr.
1	Non-preg	11	0.5227	0.4773	0.5000		
2	1st Month	12	0.4858	0.5042	0.4950	-	-
3	2nd "	8	0.5438	0.5375	0.5406	+	-
4	3rd "	6	0.4750	0.4617	0.4683	-	-
5	4th "	7	0.5423	0.5100	0.5172	-	-
6	5th "	5	0.5000	0.5200	0.5100	-	-
	Average		0.5092	0.5008			

Facing page 65.

of the uterine wall, has been undertaken and the results are presented in Tables 20 - 22.

In no instance is it possible to demonstrate any difference between the tube from the pregnant side and the opposite one. However, when the total groups are considered, significant variations are encountered. Here the last four groups are significantly longer than the first two, but show no real differences among themselves. This is illustrated in Fig.18. From the second month of gestation the tube from the pregnant side is always slightly (but not significantly) longer than the other.

Discussion. As the increase in length is not accompanied by an increase in weight, actual growth cannot account for the elongation. It is suggested that a certain amount of stretching of the tube occurs early in pregnancy when both curvatures of the horn are growing steadily. The reason why this stretching does not appear to cause a decrease in the diameter of the tube may be that the latter was measured at the middle of the length, whereas the stretching is likely to occur mainly at the uterine end of the tube. If mechanical stretching is the cause of the elongation, then the latter cannot be regarded as a true change of pregnancy, and it must be concluded that it is not possible to demonstrate that gestation has any effect on the macroscopic appearance of the Fallopian tubes.

(b) FOETAL MEMBRANES & FLUIDS.

1. MEMBRANES.

The weights tabulated in Table 23 are those of the two membranes combined. These data are presented graphically in Fig.19. The reason for the omission of Group 1 is obvious.

The membranes grow rapidly until the end of the third month; in the following month there is hardly any increase in weight, and then in the last month the rate of increase exceeds that of any of the previous months. Attention is directed to the flattening of

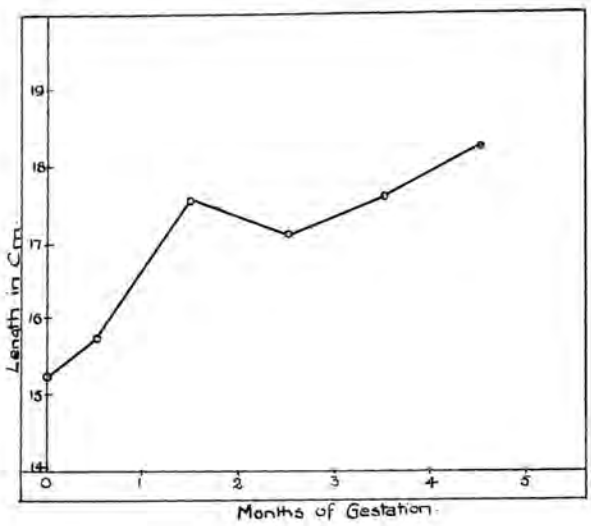

FIG. 18. LENGTH OF FALLOPIAN TUBES.

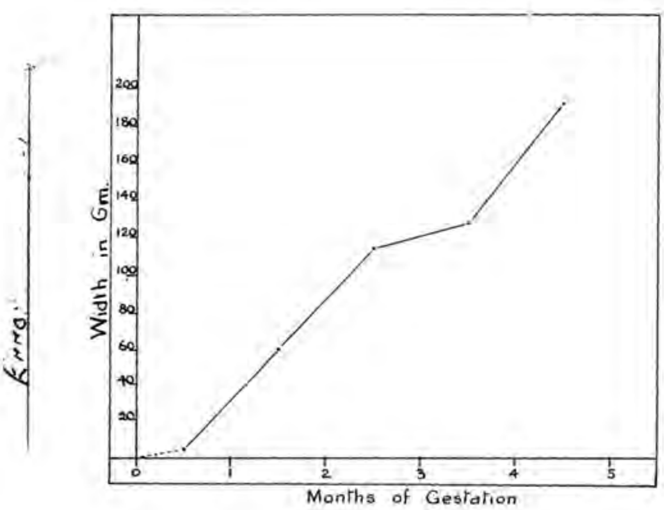

FIG. 19. WEIGHT OF FOETAL MEMBRANES.

the graph during the fourth month, this being similar to what is observed in connection with the growth of the uterus.

TABLE 23. WEIGHT OF FOETAL MEMBRANES.

Groups of Ewes. No.	Class.	No.of Ewes.	Mean Weight of Membranes.	Significance Tests. W.Gr.2.	W.Preced.Gr.
2.	1st Month	7	6.94 gm.		
3	2nd "	8	60.70 gm.	X	X
4	3rd "	6	115.58 gm.	X X	X
5	4th "	7	128.57 gm.	X X	-
6	5th "	5	192.80 gm.	X X	X

As at all times the volume of the membranes is very similar to their weight, the data for the former have not been analyzed.

Discussion: It has been seen that the membranes undergo an enormous increase in weight during pregnancy. However, the two membranes do not at all times contribute equally to this enlargement. At the 16th day of pregnancy an elongated pale membrane is seen in the pregnant horn, but it is not till the 18th day that the two sacs can be distinguished. At this time the allantois is distended with fluid and it extends almost the entire length of the gravid horn. The amnion is just visible as a narrow crescent shaped membrane closely investing the embryo which is situated towards the middle of the length of the allantoic sac. Two days later the latter sac has extended into the body of the uterus ~~for~~ and some distance along the non-gravid horn. At this stage this sac appears to be composed of a loose, velvety outer layer and a clearer inner one, in which the blood vessels seem to be located. Of the latter there are two main sets, extending from the umbilical region to each tip of the sac, and from these small branches run across the inner surface of the sac. By the 25th day the narrow, elongated allantoic sac has reached almost to the apices of both uterine horns. At this time the amnion begins to enlarge slightly, but it is not until the 30th day that it stands away clearly from the foetus.

From now on the membranes increase in size and also in thickness. The bloodvessels enlarge and their branches become more numerous. At the middle of the second month opaque white flakes begin to appear

TABLE 24. VOLUMES OF FOETAL FLUIDS.

Groups of Ewes. No	Class	No. of Ewes	Mean Vol. cc. Allantoic	Significance Tests W.Gr.1.	Significance Tests W.Preced.Gr.	Mean Vol. cc. Amniotic.	Significance Tests. W.Gr.1.	Significance Tests. W.Preced.Gr.
2	1st Month	9	24.17			1.5		
3	2nd "	8	93.63	-	-	112.69	X	X
4	3rd "	5	185.20	X	-	698.00	X X	X X
5	4th "	7	347.29	X X	-	525.71	X X	X X
6	5th "	5	762.00	X X	X X	329.00	X X	X X

facing page 67.

on the surface of the allantoic membrane. These are seen first in the region over the foetus, from where they spread towards the tips. They are never so dense as to impair seriously the transparency of the membrane. Now too the necrotic tips of the allanto-chorion are plainly visible. At the 66th day the amnion has enlarged to such an extent as to bring the central zone of its outer surface into direct contact with the overlying parts of the ~~allantois~~ chorion. Thus the ~~latter~~ allanto-chorionic space is divided into two compartments which communicate with each other, and with the urachus by means of a narrow tube-like cavity.

Until the 100th day both sacs are well filled with fluid, hence the membranes are tense. After this time the same degree of distension is apparently not maintained, so that by the end of the fourth month the sacs appear slightly collapsed. Especially is this the case with the amnion. The membranes are now relatively thick and fairly strong. Till the end of gestation they remain colourless and more-or-less transparent.

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2. <u>FOETAL FLUIDS</u>.

Details of the volumes of both the allantoic and the amniotic fluids are presented in Table 24. In Fig.20 the upper curve represents the total volume of fluid, while the lower one indicates the volume of amniotic fluid. The allantoic volume is represented by the portion lying between the two graphs. The total volume increases rapidly until the end of the third month. This is caused mainly by the amniotic fluid, which reaches its peak in the third month. Although the volume of allantoic fluid increases during this period, the rate is comparatively slow. However, in the fourth month this rate is accelerated to such an extent that the increase in the allantoic fluid is sufficient to neutralize the effect of a rapid drop in the amniotic volume, and thus in this month the total volume remains practically unchanged. In the last month the allantoic fluid is doubled and as a result of this the total volume shows a distinct rise, in spite of the continued decrease in amniotic fluid.

In Table 25 it is seen that, as regards hydrogen ion concentration,

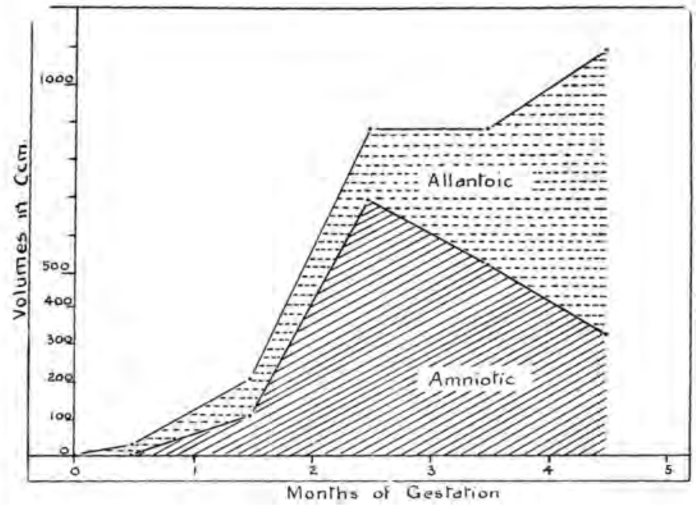

FIG. 20. VOLUMES OF FOETAL FLUIDS.
(n.b. Allantoic volume is read vertically & not at right angles to the curve.)

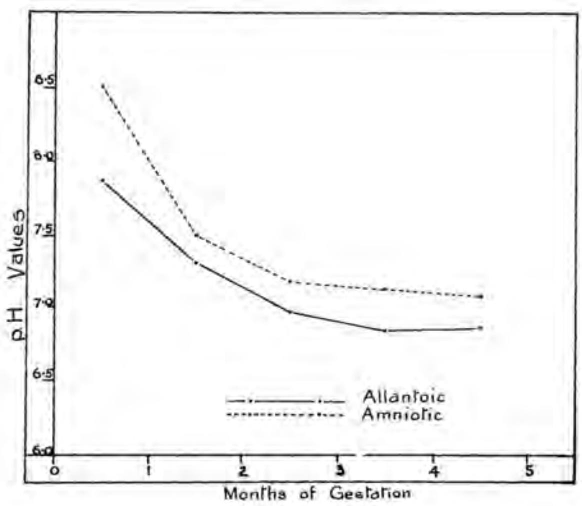

FIG. 21. HYDROGEN ION CONCENTRATION OF FLUIDS.

TABLE 25. HYDROGEN ION CONCENTRATION OF FLUIDS.

Groups of Ewes No.	Class	No. of Ewes.	Mean pH. Allantoic	Significance Tests. W.Gr.1.	W.Preced.Gr.	Mean pH. Amniotic	Significance Tests. W.Gr.1.	W. Preced.Gr.
2	1st Month	6	7.867			8.500		
3	2nd "	8	7.329	X X	X X	7.500	X X	X X
4	3rd "	5	6.960	X X	-	7.180	X X	-
5	4th "	7	6.829	X X	-	7.143	X X	-
6	5th "	5	6.860	X X	-	7.080	X X	-

Facing page 68.

there are differences between the two fluids; also in each fluid this concentration decreases with the advance of gestation. However, in both fluids, this reduction is significant only in the second month, after which the variations are slight. These facts are illustrated in Fig.21.

The specific gravity of the fluids is considered in Table 26. Due to insufficient data for the first month, Group No. 2. had to be omitted. All that may be concluded from these figures is that the specific gravity of the allantoic fluid is always higher than that of the amniotic. All other variations, even the apparent steady downward trend in the case of the amniotic fluid, are insignificant.

TABLE 26. SPECIFIC GRAVITIES OF FLUIDS.

Groups of Ewes. No.	Class.	No.of Ewes.	Mean Specific Gravity. Allantoic.	Amniotic.
3.	2nd Month	6	1.0075	1.0045.
4.	3rd "	5	1.0128	1.0042
5.	4th "	7	1.0127	1.0043
6.	5th "	5	1.0114	1.0026

Discussion:

In the failure of the total volume of foetal fluid to increase during the fourth month of pregnancy lies the explanation for the peculiar flattening observed in most of the curves dealing with growth of the uterus and its parts. Apparently to some extent enlargement of these parts is dependent upon the stretching effect of the foetal fluids. Moreover, at this time, the fluids constitute a very large proportion of the weight of the entire foetal system. These facts make it clear why in its growth the uterus should follow a course ~~as~~ resembling closely that of the increase in volume of the fluids.

Both as regards hydrogen ion concentration and specific gravity the fluids differ one from the other. In other physical properties these differences are also recognizable . In the early stages of pregnancy both fluids are clear, colourless and watery. This is maintained until the 45th day, at which time the allantoic fluid turns slightly cloudy. During the following two weeks this turbidity becomes more

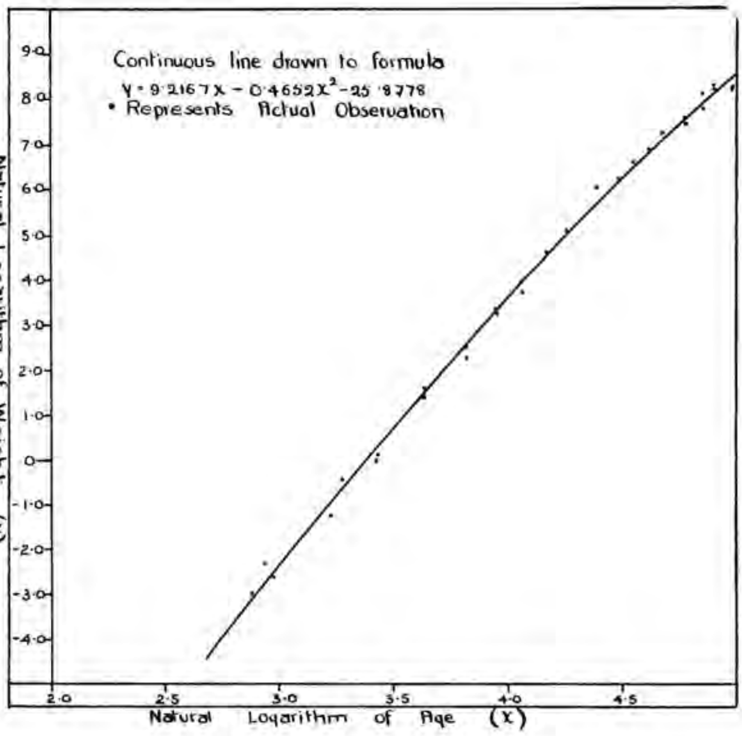

FIG. 22. **PARABOLA OF SECOND ORDER FITTED TO LOGARITHMIC VALUES OF WEIGHT & AGE DATA.**

pronounced and a lemon tinge appears in the previously colourless fluid. This becomes more intense, and then gradually changes to amber. At the 81st day it is difficult to decide which of the two colours is present, but a week later there is no longer any doubt. The bright amber colour then seen darkens into a golden brown, which shade is encountered throughout the remainder of the period. The turbidity previously mentioned increases until the end of the third month, as does the viscosity. During the last two months the fluid again becomes watery, clear and practically transparent.

In the amniotic fluid the lemon tinge is visible at the 52nd day. Within a short time it has changed to amber, but the latter shade is never very deep. During the fourth month the amber colour disappears and the fluid acquires a very light green colour. In the meantime the viscosity and the turbidity have increased so that by the end of the fourth month the amniotic fluid is thick and "syrupy" and very cloudy. The colour varies from a pale green to a dirty white. During the later stages a fair amount of meconium is found in the amniotic fluid.

(c) FOETUS.

All details regarding age, weight and dimensions of the entire series of foetuses are presented in tabular form in Appendix A. The trends of the growth processes exhibited by these observations are best studied through the process of curve-fitting. In order not to complicate the text with statistical technicalities all details of the procedure adopted have been relegated to Appendix B_1. ~~where worked examples are set out in full~~.

1. GROWTH IN WEIGHT.

MacDowell *et al* (1927) maintain that when for a series of foetuses the natural logarithms of age are plotted against those of the corresponding weights a straight line distribution results. However, in their work age is calculated not from the moment of

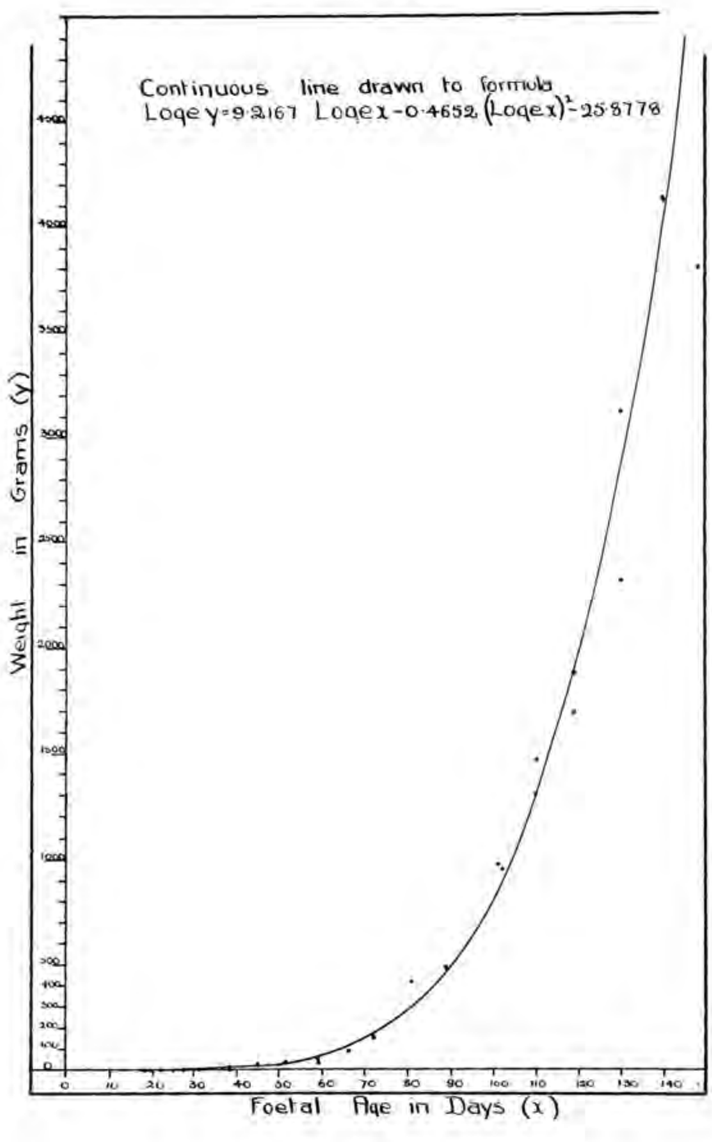

FIG. 23. PARABOLA OF SECOND ORDER FITTED TO ACTUAL VALUES OF WEIGHT & AGE DATA.

fertilization of the ovum, but from the time of formation of the "embryo proper." X So distinct is the linear trend of the data in Fig. 22 that one is led to surmise that, in spite of the difference in the method of computation of age, here too the general type of MacDowell's formula will hold good. Moreover, it is possible to fit such a parabola (of the first order) to the data and to obtain a result significant at 1% probability. Nevertheless, the points representing the actual observations are not evenly scattered about this straight line. When, by the use of anti-logarithms, a weight-age curve is constructed from the formula it becomes quite evident that the formula in question does not give a good representation of the trend of the data. Towards the latter end of the period the curve rises much too steeply and thus passes well to the left of all the actual observations.

In view of the above it becomes necessary to test the "fit" of a parabola of the second order. The regression formula obtained is :--

$$\text{Log}_e \text{ Wt} = 9.2167 \text{ Log}_e \text{ Age} - 0.4652 (\text{Log}_e \text{ Age})^2 - 25.8778,$$

and the continuous line in Fig. 22 is drawn from it. Both factors b_1 and b_2 (see Appendix B) are highly significant (at $P = .01$), while the coefficient of variation is 20.07%, which is 4% lower than that of the straight-line formula. Both in Fig 22, and in the weight-age curve in Fig. 23, the actual data are well scattered around the curves, indicating that the formula from which these curves are constructed gives a true representation of the trend of the data. The figure for the coefficient of variation (20%) is still high, but, in view of the large variations in the original data (see differences in weights of foetuses of identical age) this is only to be expected. Fitting to a further degree will certainly not bring about any improvement and will only serve to complicate the formula.

It is ~~concluded~~ concluded that the age and weight data obtained from the series of Merino foetuses are best fitted by a parabola of the second order. This type of formula produces a curve with two inflections,

---

X Probably the stage with the primitive axis established and with the formation of somites just commencing.

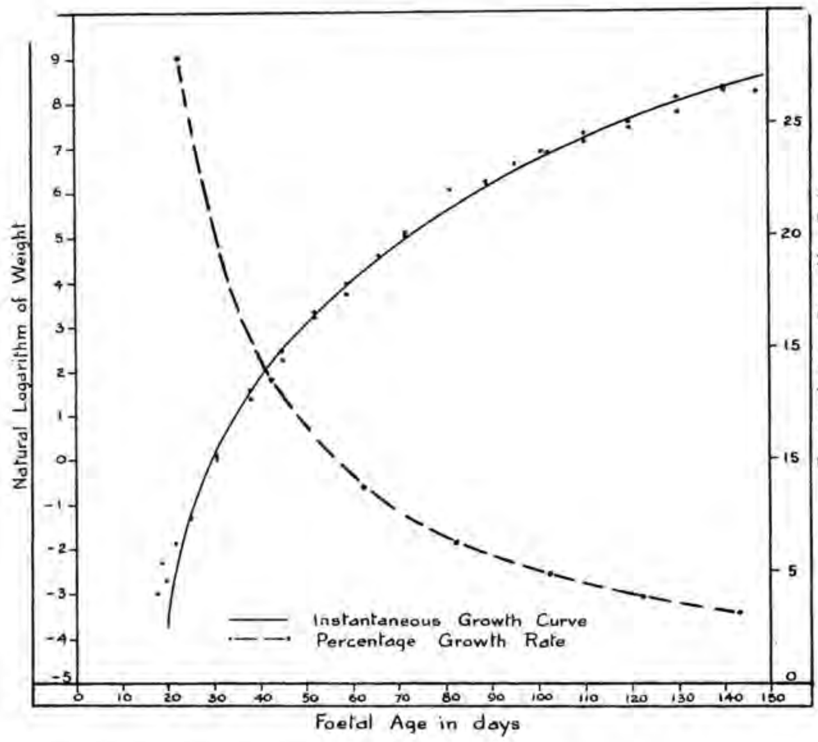

FIG. 25. TWO CURVES TO INDICATE THE DISTRIBUTION OF $\log_e$ WEIGHT AGAINST AGE, & RELATIVE PERCENTAGE GROWTH-RATE CALCULATED ON A DAILY BASIS AT TWENTY DAY INTERVALS.

fallacious computations so often encountered in works of this nature, it is essential to remember that, by virtue of the constantly changing mass of the growing foetus, it is impossible to arrive at a true determination of the percentage growth-rate through any calculation based upon the "simple interest" conception. The errors introduced by such methods are exposed by Brody (1927a) who shows that the rates mentioned by Minot (1908) are all too high, and that the exaggeration is greatest when the rate is highest and when the time interval between successive observations is long.

The growth process is best likened to the increase of capital set out at interest which is being compounded instantaneously i.e. the increment for one instant forming part of the capital for the following instant. However, the rate of interest (which is the percentage growth-rate) does not remain fixed, but is subject to change during the course of prenatal life.

Brody (1927a) appears to have been the first investigator to appreciate these facts. By recourse to the calculus he is able to demonstrate that the graph resulting from the plotting of the natural logarithms of weight against age actually represents the trend of the instantaneous growth-rate, and that the slope of the curve at any point is an indication of the growth-rate at that moment.

From the data at his disposal Brody (1927b) concludes that such instantaneous growth-rate curves are composed of several segments set at varying and decreasing slope. Thus he maintains that the growth-rate remains steady over a considerable period and then changes abruptly to a lower level.

In Fig. 25 is presented the curve for instantaneous growth of the Merino foetus. The dots represent the actual observations, while the continuous line is drawn through points obtained by plotting weight values calculated from the formula previously mentioned. It is observed that the resulting graph is a smooth curve concave to the axis of the figure. This is contrary to Brody's findings for here there is no evidence of straight segments. Here the decrease in the rate of growth is spread evenly over the entire ~~period~~ term and is not limited to certain very short and well defined periods. It is hardly likely that the difference in these findings is attributable to the species on which the observations have been made. Not only does Brody's work cover a wide range (the rat, the guinea-pig, the chick and man) but also regarding the bovine similar results are claimed by Kislovsky & Larchin (1931.) On the other hand, in their work on the mouse, MacDowell et al (1927) present a curve almost identical with that in Fig. 25. There is much point in these authors' criticism of Brody's work, namely that the data on which he relied were unsatisfactory, and that he failed to realise that any curve may be approximated by a series of straight lines. Both Brody and Kislovsky & Larchin merely plot their data on arithlog paper and then draw their straight lines by inspection. Brody (1927a) actually claims for this method the special merit of keeping the normal trend of the data more prominently under consideration, as compared with the tendency in the method of least squares of stressing the deviations from this normal trend. However, his arguments do not appear to affect the present situation, in which both the actual data and the "fitted" data are plotted. When it is observed that the numbers of observations in Brody's and in Kislovsky & Larchin's works are limited, and that there are fair deviations from the actual lines drawn, then it must be realised that their conclusions are open to criticism.

It is significant that in the present investigation and in MacDowell's work, where efforts have been made to limit the factors likely to cause variations in foetal weight, and where relatively large numbers of observations have been recorded, smooth curves are obtained. Further, it is apparent from Fig. 25 that when the chance deviations from the general trend are eliminated then the plotted points all fall directly on a smooth curve.

It must be concluded that the weight of evidence is against the occurence of abrupt "breaks" in the growth-rate. In the sheep definitely (and most probably in other mammals too) the rate decreases in a steady and regular manner throughout the course of prenatal life.

The instantaneous relative growth-rate (designated K) may be calculated on a daily basis from the following formula :--

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The instantaneous relative growth-rate (designated K) may be calculated on a daily basis from the following formula :--

formula should read = 6.1145 $Log_e x$ - 0.4901 $(log_e x)^2$ - 14.4240

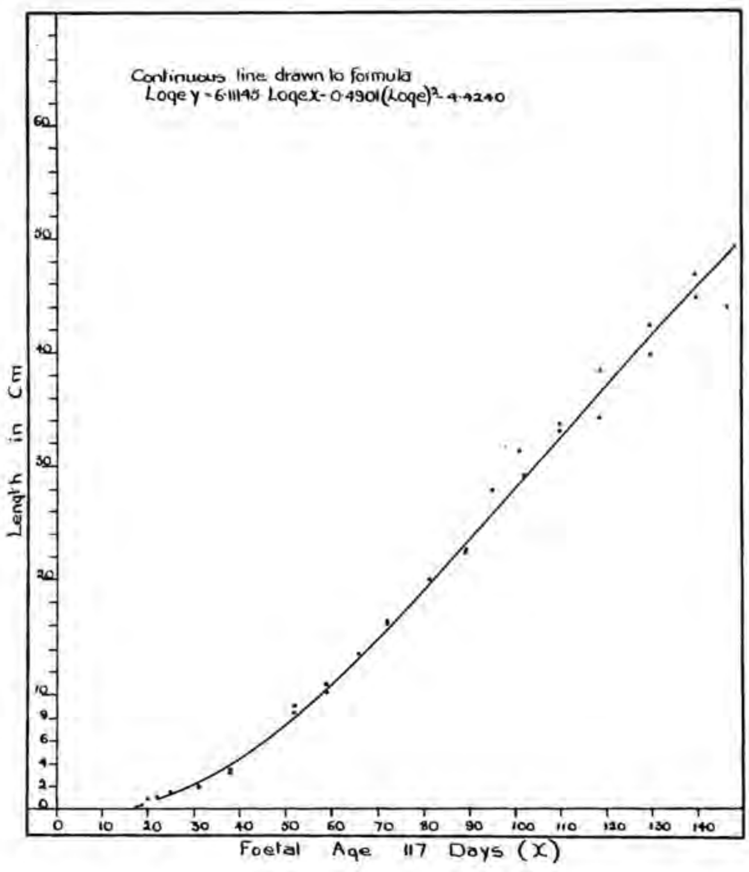

FIG. 26. PARABOLA OF SECOND ORDER FITTED TO THE ACTUAL VALUES OF STRAIGHT CROWN-RUMP LENGTH & AGE.

$$K = \frac{\text{Log}_e W_2 - \text{Log}_e W_1}{T_2 - T_1}$$

where W_2 & W_1 are the foetal weights at the ages T_2 & T_1 days respectively.

The figure obtained is an average value over the period T_1 to T_2 days. As it has been noted that the rate of growth is changing continuously the value obtained will vary somewhat with the length of the period $T_2 - T_1$. The amount of variation will not be large. However, for comparative purposes it will be better to keep the period constant for all such calculations.

By multiplying the value of K by 100, the rate may be expressed as a percentage, - thus :--

Instantaneous (Average) Percentage rate per day = 100 X K

$$= \frac{\text{Log}_e W_2 - \text{Log}_e W_1}{T_2 - T_1} \times 100$$

In Table 27 are tabulated such percentage rates calculated over periods of five days at twenty day intervals throughout the foetal period.

TABLE 27. GROWTH-RATES. - PERCENT. PER DAY.

Age - days.	Value of K	% per day.
20 to 25	0.2824	28.24%
40 " 45	0.1350	13.50
60 " 65	0.0860	8.60
80 " 85	0.0620	6.20
100 " 105	0.0479	4.79
120 " 125	0.0387	3.87
140 " 145	0.0323	3.23

The table indicates clearly that the percentage rates calculated by Minot (1908) and others, which run into several hundred percent., are excessively high and that the drop in the earlier stages is not nearly as exaggerated as these workers lead one to expect. The rates are comparable with those calculated by Brody (1927b) for the rat (53%), the guinea-pig (10% to 4.6%) and the human being (8% to 1.25%). It is also interesting to note that Brody (1927b) calculates

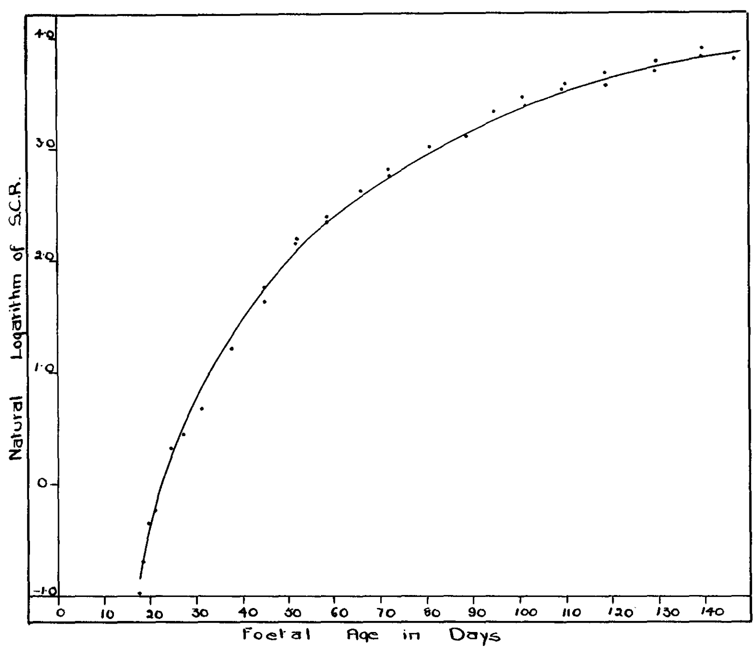

FIG. 27. DISTRIBUTION OF $\log_e$ STRAIGHT CROWN-RUMP LENGTH AGAINST AGE. (SMOOTH CURVE DRAWN THROUGH POINTS OBTAINED BY CALCULATING ABSCISSAL READING FROM REGRESSION FORMULA).

the percentage daily growth-rate of the sheep during the first few weeks of postnatal life to be approximately 2%, which is only slightly lower than that given above for the 140 - 145 day period, thus lending weight to the contention that the incident of birth is not accompanied by any drastic change in the growth-rate.

2. GROWTH IN LENGTH.

In view of the conflicting opinions as to the best method of determining the length of foetuses, and the fact that these opinions all rest upon a theoretical basis, it has been decided to consider here a few of the most usual methods, and from the results of statistical tests to conclude which are the most useful as a guide to foetal linear development. All the dimensions considered are described in Chapter 3.

The data for straight crown-rump length are best fitted by a second order parabola having the formula :--

$$\text{Log}_e\ \text{C.R.(s)} = 6.1145\ \text{Log}_e\ \text{Age} - 0.4901\ (\text{Log}_e\ \text{Age})^2 - 14.4240$$

This curve is definitely significant at the 1% level of probability, while the coefficient of variation is 7.51%. In Fig. 26 it will be seen that the data are well distributed about this line. Further, it is noticed that the second inflection is not very distinct and that the curve does not resemble an elongated "S" as stated by Curson & Malan (1935). However, it approximates fairly closely to Draper's (1920) guinea-pig curve.

In Fig. 27 is presented the instantaneous growth-rate curve of straight crown-rump length. Again the curve is smooth, without any abrupt breaks, and lies concave to the axis of the graph. In general shape it conforms closely to that of the weight data.

Details of the percentage growth-rate of this dimension are tabulated in Table 28. It is noticed not only that this rate is lower at each stage than that of the weight, but also that the decrease in the rate towards the end of foetal life is much more exaggerated here. As a result of this greater "slowing down" in linear growth the second inflection of the growth curve has been appreciated by workers who have failed to detect its existence

Last term of formula should read - 9.7855

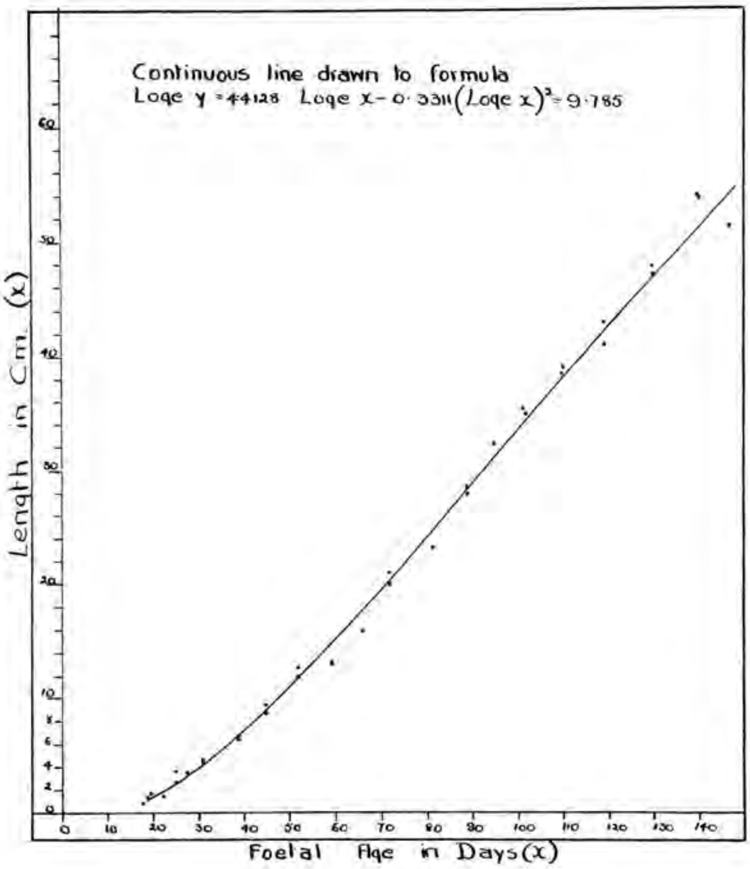

FIG. 28. PARABOLA OF SECOND ORDER FITTED TO ACTUAL VALUES OF CURVED CROWN-RUMP LENGTH.

in connection with weight data.

TABLE 28. GROWTH RATES - C.R.(S) % PER DAY.

Age - Days	Value of K.	% per day.
20 to 25	.1370	13.70.
40 " 45	.0575	5.75
60 " 65	.0330	3.30
80 " 85	.0217	2.17
100 " 105	.0154	1.54
120 " 125	.0114	1.14
140 " 145	.0088	0.88

The second dimension to be considered is Curson & Malan's (1936a) curved crown-rump length. The best-fitting curve is a parabola similar to those already considered. The formula is :--

$$\text{Log}_e \text{ C.R.(c)} = 4.4128 \text{ Log}_e \text{ Age} - 0.3311 (\text{Log}_e \text{ Age})^2 - 9.7855.$$

Although the significance is marked, the coefficient of variation is 10.34%. In Fig. 28 the data are less evenly distributed than those of the straight crown-rump length. Thus one concludes that in spite of the theoretical advantages of the curved over the straight line, the latter, when measured according to a set plan, is the less variable and hence the more useful of the two. This had already been indicated in the work of Curson & Malan (1936a) in whose weight-length diagrams the curved measurement gave a less satisfactory "fit" than that obtained with the straight line dimension.

Undoubtedly a fair proportion of the variation of this measurement is directly attributable to the difficulty of taking precise readings when one of the landmarks is as vague as the " root of the tail." Apart from this technical difficulty there is the fact that this dimension is affected not only by growth in the direction of the long axis of the body, but also by growth at right angles to this axis i.e. in the length of the head. It is difficult to see how such a "composite" line can be expected to represent satisfactorily the linear enlargement of the body.

In order to avoid the above criticism the head portion of the curved line has been omitted in the measurement of the back-line. The data obtained are plotted in Fig. 29, in which the

~ right side first term should read 4·1210

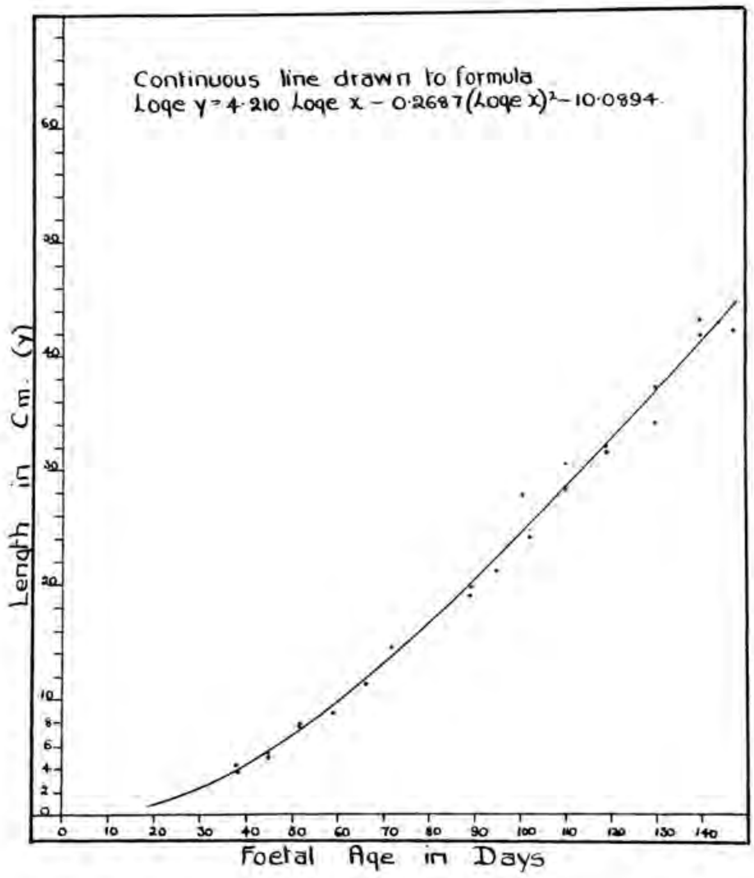

FIG. 26. PARABOLA OF SECOND ORDER FITTED TO ACTUAL VALUES OF BACK-LINE.

continuous line has been drawn to the formula:--

$$\log_e \text{Back-line} = 4.1210 \log_e \text{Age} - 0.2887 (\log_e \text{Age})^2 - 10.0894$$

This formula is highly significant even at the 1% level of probability. In this instance the coefficient of variation is 4.93%, which must be regarded as extremely satisfactory. However, in the determination of this dimension the root of the tail is again the caudal landmark. Consequently it is not surprising to find that by measuring the length of the entire vertebral column (i.e. the foregoing length plus the tail) the coefficient of variation can be reduced to 3.8%. The formula here is :--

$$\log_e \text{V.C.} = 4.3948 \log_e \text{Age} - 0.2949 (\log_e \text{Age})^2 - 10.4383$$

The tests for significance yield positive results at the level of $P = .01$

This dimension differs from Mall's (1910) "vertebral column length" for the human being in that in the latter the length of the tail is disregarded. In the sheep foetus the tail is relatively long, hence, perhaps, its greater importance. However, it appears that the slight superiority of the vertebral column length over the back-line is the result of greater accuracy in the measurement of the former, due entirely to the fact that in this case both landmarks are specific.

In Table 29 are tabulated details of the percentage growth-rate of the vertebral column length. The corresponding figures for the back-line resemble these very closely.

TABLE 29. V.C. LENGTH. PERCENT. RATE.

Age - Days	Value of K.	% per day.
20 to 25	0.1094	10.94
40 " 45	0.0496	4.96
60 " 65	0.0304	3.04
80 " 85	0.0212	2.12
100 " 105	0.0159	1.59
120 " 125	0.0126	1.26
140 " 145	0.0102	1.02

In Fig 31 is presented the instantaneous growth-rate curve of this dimension. The actual observations follow very closely the

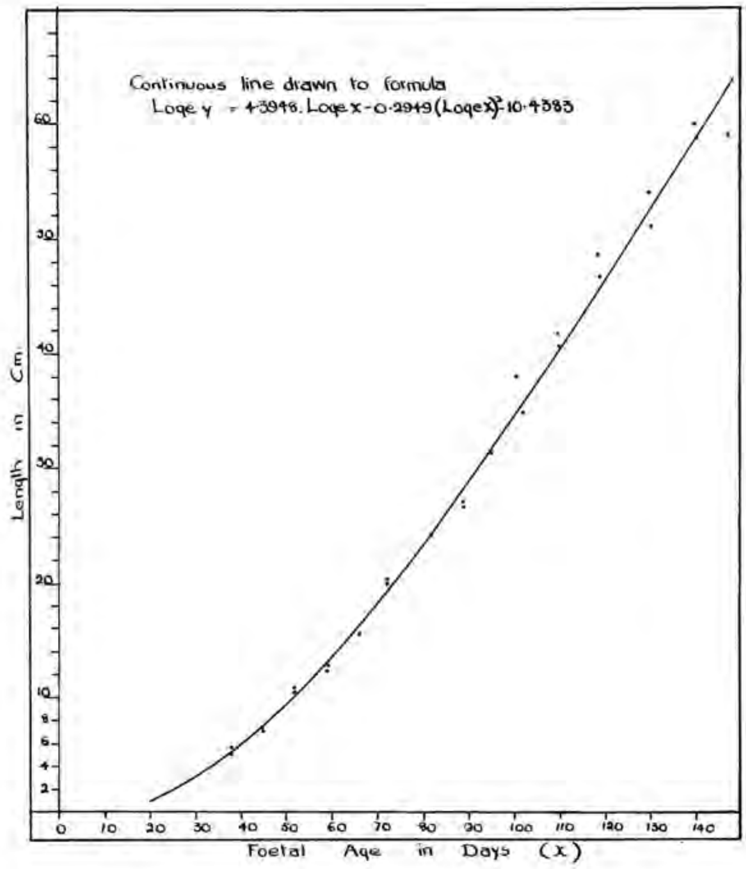

FIG. 30. PARABOLA OF SECOND ORDER FITTED TO THE ACTUAL VALUES OF VERTEBRAL COLUMN LENGTH.

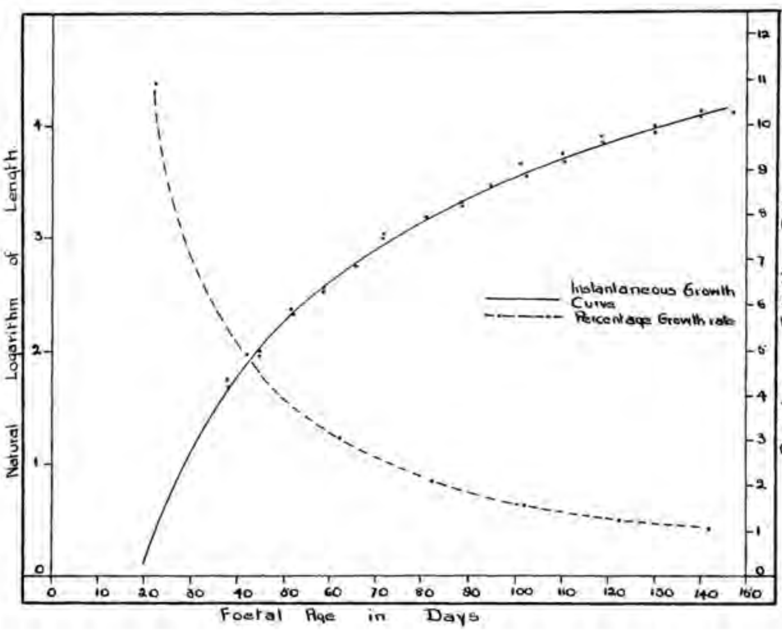

FIG. 31. TWO CURVES TO INDICATE THE DISTRIBUTION OF Log_e VERTEBRAL COLUMN LENGTH AGAINST AGE & RELATIVE PERCENTAGE GROWTH-RATE CALCULATED ON A DAILY BASIS AT TWENTY DAY INTERVALS.

smooth curve drawn from calculated lengths. Again there is no suggestion whatsoever of straight segments with sudden "breaks." The shape of the curve is similar to that obtained with the weight data; so too is the graph of average percentage growth-rates which is also plotted in Fig. 31.

It is found that the trend of growth in all four of these linear dimensions is best represented by parabolae of the second degree. In no instance is the second inflection at all distinct. There is a fair degree of similarity in the average percentage growth-rates of these dimensions and at each period they are all well below the rate of growth in weight.

Considering the coefficients of variation of these lines it is found that the vertebral column length and the back-line are the least variable, and hence the most useful dimensions. The straight crown-rump length is slightly inferior to them, but it is especially useful in connection with foetuses younger than 35 days, in which the first two dimensions cannot be determined with any degree of accuracy.

The curved crown-rump length is definitely the least useful of the measurements considered and, remembering the other criticisms of this line, it may be discarded.

It is to be noted that the coefficient of variation of this discarded line is only half that of the weight-curve, while regarding vertebral column length this fraction is reduced to one-fifth. These findings are contrary to the assertion of Curson & Malan (1936a) that "weight and length are equally variable." Hammond's (1927) statement that "weight is more variable than length" is applicable with equal force to the foetal, as well as the post-natal period of animal life.

3. "<u>WEIGHT-LENGTH RATIO</u>."

In studying the Weight-Age and Length-Age curves just described it is found that when the weight of a particular foetus lies above the trend line, the point representing the length of that foetus also tends to fall above the smooth curve. This suggests that there may be a distinct correlation between these two

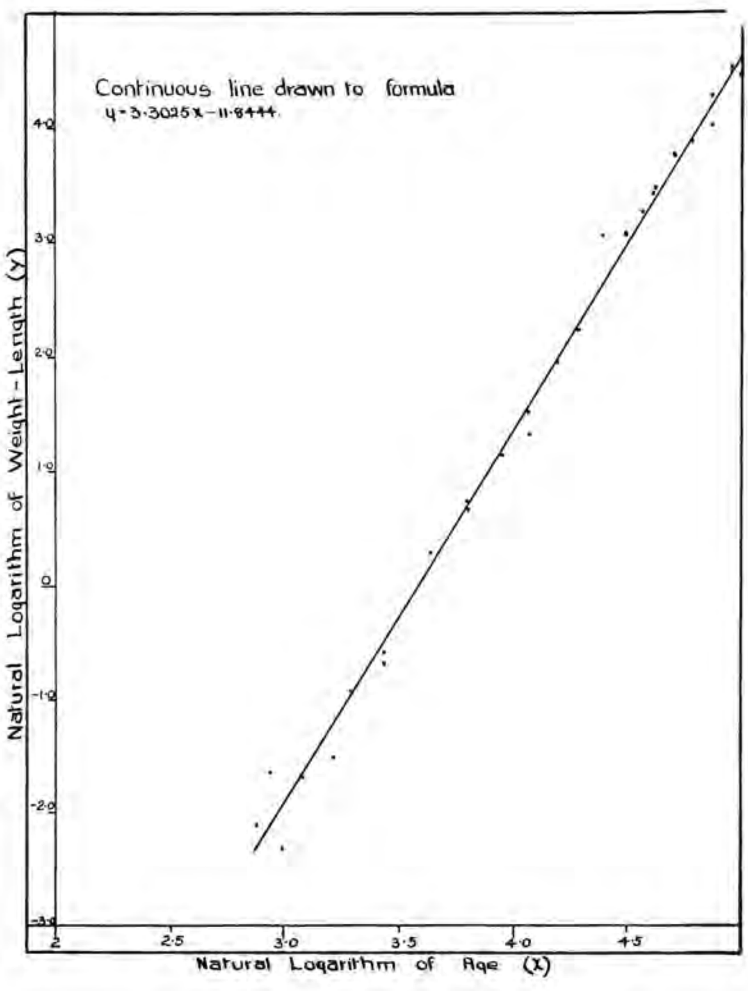

FIG. 32. STRAIGHT LINE RESULTING FROM THE PLOTTING OF THE LOGARITHMIC VALUES OF WEIGHT-LENGTH RATIO AGAINST AGE.

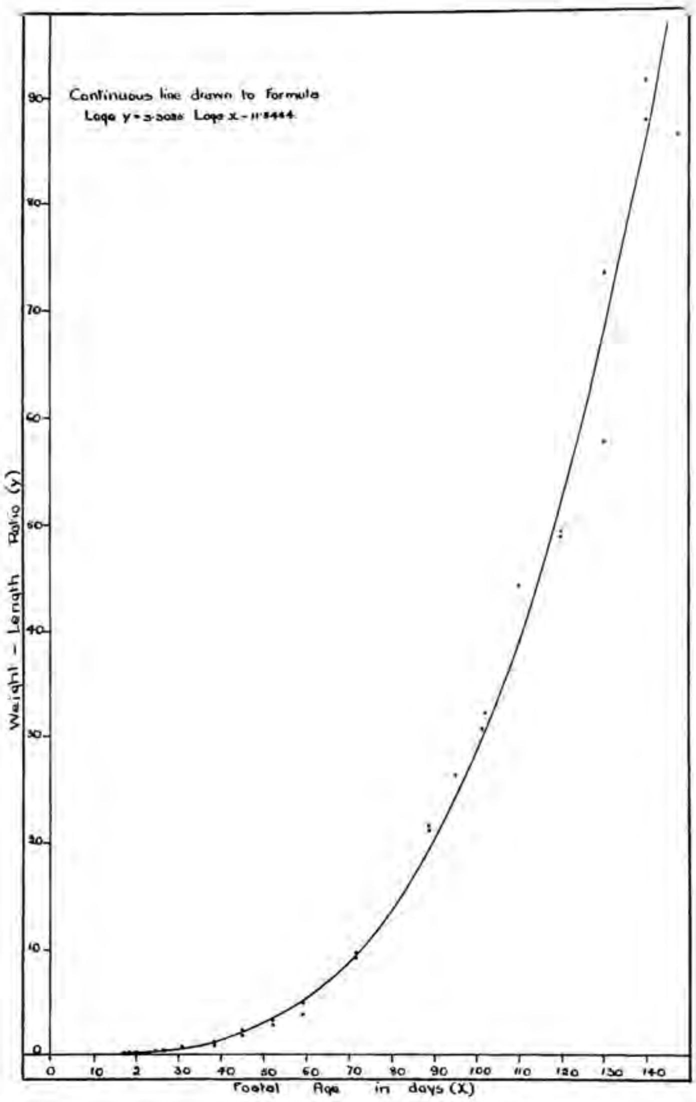

FIG. 33. PARABOLA OF FIRST ORDER FITTED TO THE ACTUAL VALUES OF WEIGHT-LENGTH RATIO AND AGE.

characteristics and that it may be profitable to calculate for each foetus the weight-length ratio, and to study the trend of this ratio with a view to determining whether it would not prove less variable than either of the two dimensions from which it is calculated.

Although it has been proved that the length of the vertebral column is the least variable of the length measurements it is felt that, on account of its total disregard of the head, this dimension is not the most suitable for the purpose of calculating a weight-length index. Consequently, the straight crown-rump length is preferred, and in each instance this measurement in centimetres is divided into the weight in grams.

In Fig. 32 it is shown that the plotting of the natural logarithms of these indices against those of the corresponding ages results in a straight-line distribution. The continuous line in the figure is drawn to the formula :--

~~Log~~

$$\text{Log}_e \text{ W. L. Ratio} = 3.3025 \text{ Log}_e \text{ Age} - 11.8444,$$

which is highly significant, but has a coefficient of variation of 17.3%. It is quite evident that the computation of this index will not serve any useful purpose.

Figure 33 is inserted mainly to indicate that the formula mentioned does actually represent the true trend of the data and that the large coefficient of variation is due entirely to occasional marked deviations from this general line.

4. REGIONAL GROWTH.

Growth of the body as a whole is merely the sum total of growth of all its component parts. If the rates of growth of all these parts were identical, the body would increase in size without in any way changing its shape or its proportions. However, it is well known that this is not the case, and that growth and moulding of shape proceed hand in hand. Regarding the sheep foetus this is well illustrated in an admirable chart presented by Curson & Malan (1935). Here outline sketches

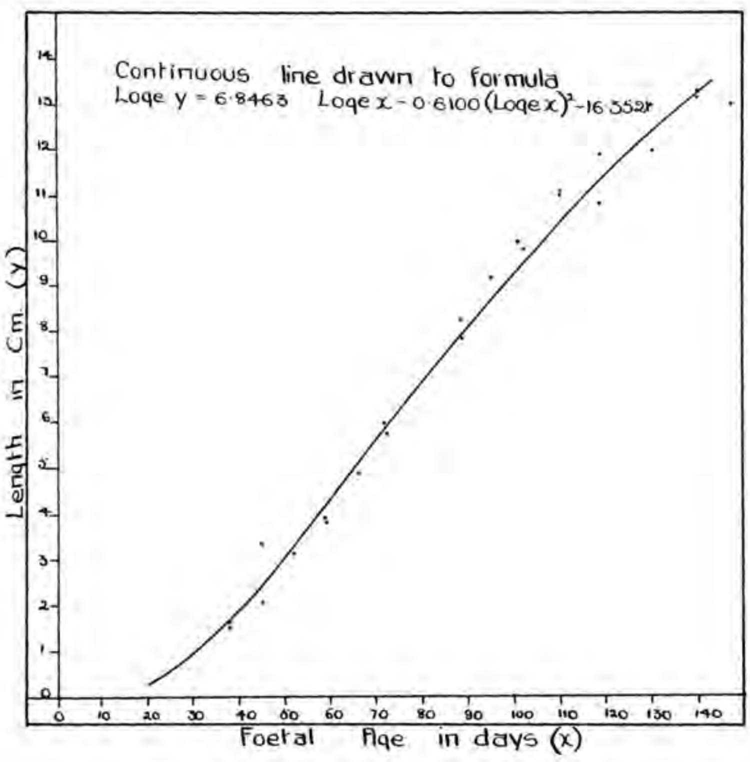

FIG. 34. PARABOLA OF SECOND ORDER FITTED TO ACTUAL DATA OF LENGTH OF HEAD & AGE.

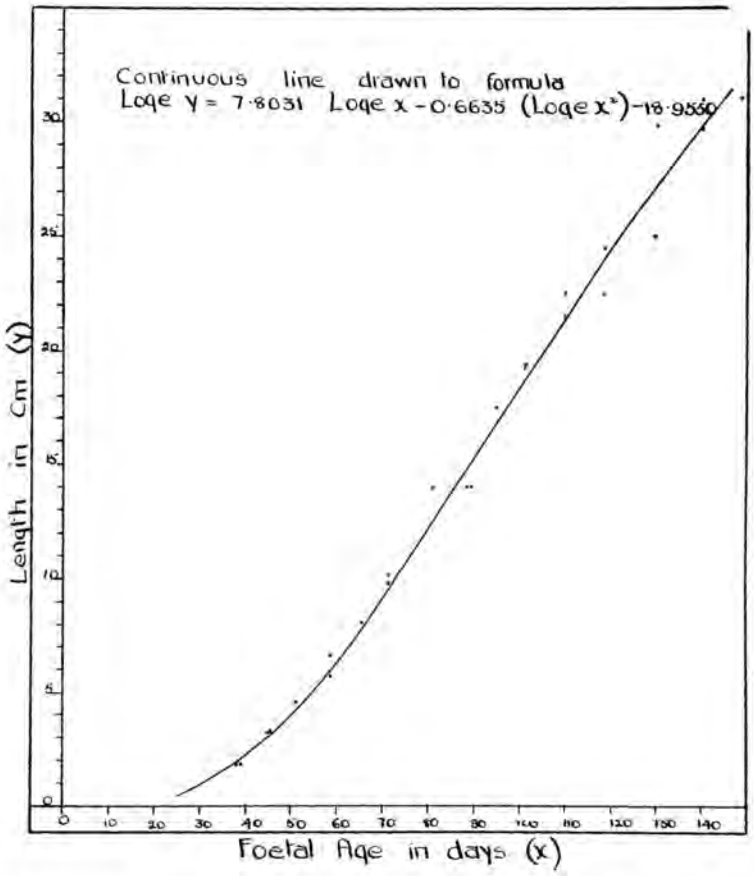

FIG. 35. PARABOLA OF SECOND ORDER FITTED TO ACTUAL DATA OF LENGTH OF TRUNK & AGE.