612.647:612.21

THE GENESIS OF RESPIRATORY MOVEMENTS IN THE FŒTUS OF THE SHEEP

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(*Received May* 4, 1936)

In a previous paper by Barcroft, Barron & Windle [1936] a description was given of the integration of the earliest individual movements into a mass movement. In the present paper that movement, as we understand it, will be described more particularly, and an account will be given of the derivation from it of movement of the type familiar in ordinary mammalian respiration.

The experimental procedure is as given in the paper quoted above. The mass movement is well seen in sheep embryos of 36–37 days (27–29 mm. crown-rump length), and may be evoked by touching the nose with a glass rod. This may be done, if the rod is a fine one, without letting any considerable quantity of fluid out of the membranes. Here as elsewhere, unless it is otherwise stated, the observations recorded are with the embryo inside the membranes. We were always careful to note the colour of the blood in the cord, and the results given apply to experiments in which that was satisfactory. The pulse in most cases was counted. The mass movements are seen under urethane anæsthesia or with the mother under a spinal anæsthetic.

The next stage in the development of the respiratory movement follows very shortly. The movement does not alter in type; instead of being a single mass reaction, evoked by a specific stimulus or perhaps two such reactions in quick succession, it becomes definitely rhythmic, a group of movements appearing and petering out; the rate of the rhythm being usually 30–45 to the minute, though the group of movements dies away after perhaps half a minute. The youngest fœtus in which we saw this phenomenon was aged 38 days and was 31 mm. in length.

"Ewe was under light urethane anæsthesia, 3 c.c. per kg. and the uterus delivered into the bath at 40° C." and the fœtus was exposed in the intact amnion. "There were no spontaneous movements until after the fœtus had been exposed some time....The head appeared to be extended, the trunk straightened and the limbs and tail extended. These appeared rhythmically—a sharp contraction and rather a slow relaxation. On one occasion they were definitely initiated by extension of the hind foot of the left side with abduction of the toes. This rhythmic extension and relaxation of the leg occurred several seconds before the generalized extension took place."

The rhythm described above is spoken of as spontaneous. This description must not be insisted upon except to distinguish it from the movements previously described, which were elicited only as the result of the rather forceful application of a glass rod to the surface of the embryo. Actually the rhythm of which we are now speaking made its appearance shortly (perhaps half a minute, but the time was not regular) after the application of a glass plate to the surface of the amnion for purposes of photography. It seemed likely that the movements were caused by the presence of the plate. That they were due to associated thermal or luminary effects was ruled out, and it was probable, though not proven, that they were due to the pressure of the plate.

The rate of the "rhythm" bore no relation to that of the rhythm of the mother's respiration. Nor was it that of the fœtal pulse as is shown by the following table.

TABLE I

Serial No. of sheep	Fœtal age (days)	Rate of fœtal rhythm per minute	Fœtal pulse rate per minute	Anæsthetic administered to mother
66	40	33	164	Urethane
103	41	42	162	Spinal
61	42	20	84–128	Urethane
67	43	30	—	,,
121	43	32*	126	Spinal
82	44	48	—	Urethane
85	45	36	—	,,
122	45	44	120–124	Spinal
96	46	42	128	Urethane
100	48	66	192	Spinal

* Later 48 irregular.

It must provisionally be taken as accidental that in sheep 66, 103, 96 and 100, the figure of the respiratory rate is within the limits of counting an aliquot part of the pulse rate. The two were not counted simultaneously.

No one who has seen both can fail to be struck with the similarity between these mass movements and the gasps which occur at the late stages of poisoning by inhalations of minimal lethal doses of hydrocyanic acid vapour.

The conversion of this rhythmic mass movement into movements of a more normal respiratory type is simply a process of "whittling" down.

In general the extensor movements go before those of the flexor type. The mouth ceases to open rhythmically. The neck movements undergo an interesting change about the 40th day. At first the head is simply thrown back during each mass movement. The question of the mechanism we leave open. Possibly both flexor and extensor muscles are involved and that the observed extension is the algebraic sum of their effects. Or it may be that extensor muscles only are involved. But on the 41st day, as was pointed out to us by Dr Windle, the head movement is a diphasic one, an extension of the neck succeeded by a flexion.

The next stage is for the extensor phase to drop out, leaving only the flexor phase. The method of disappearance of the former is interesting. It does not fade out by becoming progressively less powerful, but appears intermittently and at rarer intervals.

"*Sheep No.* 110—41 *days—length* 40 *mm.* Immediately (on opening uterus) rhythmic movements were seen....Each movement involved a flexion of the neck, but occasionally this was preceded by an extension of the neck. Sometimes there would be two, sometimes three flexions without extension to each flexion. The extension seemed sharper than the flexion."

Thus the general rhythm is never broken. These movements were particularly well seen in sheep No. 66, age 40 days, in which rhythmic movements of the diaphragm were also well marked as an associated part of the general rhythm. (Subsequent dissections showed that the diaphragm is complete on the 39th day.) These movements of the diaphragm of course mean that the ribs are drawn in and the liver depressed.

"*Sheep No.* 61, *age* 42 *days.* The embryo was executing rhythmic movements: they involved descent of the liver, opening of the mouth, flexion of the head and contraction of the infrahyoid muscles, as in panting."

Between the 40th and 45th days the active limb movements disappear also and the legs, in so far as they do move, only do so passively as the result of the trunk movements.

By the 46th day all rhythmic spasms have become reduced to movements of the trunk only. By this time the diaphragm is fully formed, and perhaps the most obvious phenomenon is the rhythmic depression of the liver due to the contraction of the diaphragm. The ribs are drawn in, presumably from this same cause, the chest being of course closed and the walls soft. In appearance the fœtus differs little from that of an ordinary animal which is breathing except for the drawing in of the ribs as described.

Spontaneity of the rhythmic movements

We have already stated that when first seen the movements seemed to depend upon some as yet ill understood stimulation of the fœtus. Up to the 49th day it was, however, more and more easy to elicit the rhythmic movements, so long as the fœtus was in good condition, and indeed they were elicited so easily on that day that it was very difficult to abolish them completely. The embryo presented the appearance of an animal which was breathing continuously; but the more quietly the preparation was held the slower and shallower the rhythm. The question naturally arose: if at this stage the embryo were not interfered with at all would it display rhythmic movements of the respiratory type?

To test the matter more closely without opening the uterus, we transilluminated it with a single light. Under these circumstances it was possible not only to see the shadow of the fœtus, but also its movements. At times these were certainly rhythmic, but even under these circumstances it cannot be claimed that the fœtus was entirely undisturbed; usually some manipulation of the uterus was required to bring the shadow into a position in which it was best seen. It must be remembered, on the other hand, that the fœtus is small relatively to the sac of fluid which contains it, and within the limits imposed by the length of the umbilical cord was free to move about much like a fish in a bowl.

The relation between the rhythmic movements and other muscular movements

For the most part, in what we have said above we have been dealing with movements associated with the minimum degree of interference to the fœtus. We observed incidentally that on the 49th day the more quietly we held the fœtus the slower and shallower was the rhythm. The reverse was true: muscular movement was associated with an increase both in frequency and power of the rhythm. Not only so, but the movement became more extensive, the head flexed and the infrahyoid muscles contracted. In sheep No. 101 when breathing forcibly the mouth also opened, whilst when making gentle respiratory movements it remained shut. The mass movement has been shorn of the head and limb movements between the 40th and 49th day: these movements have not been lost, but they have developed along their own lines and can be evoked by an appropriate stimulus. In particular they have assumed a relation to gravity, so that on the 49th day, if the fœtus be on its side and be

given a sharp tap either on the nose or the tail region it will perform a movement which bears a general resemblance to an effort to get up. This development of righting movement will form the subject of a later paper by one of us [Barron]. We mention it here only to say that with it is associated the increase both in rate and power of the rhythmic movements, so that the appearance presented is that of an animal which makes an effort to rise from the ground and is out of breath as the result.

Causal relation between muscular effort and rhythmic movements

It would be natural to assume as a provisional hypothesis that the acceleration of the rhythmic movements was due to the effect on the brain of blood impoverished in oxygen or enriched in carbonic acid by the muscular effort. About this theory there are several difficulties. The first is that the effect on the respiration is immediate: the second that no proof exists of this assumed asphyxial condition of the blood: and the third that an asphyxial flow does not at this stage (i.e. up to the 49th day), elicit this rhythm.

The first statement rests on inspection of the fœtuses themselves and of the films which we have taken of the phenomena concerned. With regard to the second, it must not be forgotten that this fœtal circulation is peculiar: between the time that a sample of blood traverses one of the contracting muscles and the time it reaches the brain, it (or most of it) will have traversed the placenta, where it will have had every opportunity of losing any additional carbonic acid which it may have acquired in the muscles.

As regards the third point, we have on many occasions between the 40th and the 49th days stopped the circulation in the umbilical cord. This procedure has never elicited respiratory movements; usually it has had no effect other than to prejudice the nervous system and temporarily to slow the heart. Sometimes it has caused an extension (not rhythmic) of the limbs. Once on the 49th day it produced a rhythmic chewing movement, but never in our experience has clamping or tying the cord within the first 49 days elicited the rhythm of the respiratory type which forms so striking a feature of fœtal life at that time.

The accentuation of this rhythm contingent on muscular effort seems not to be associated with the chemical regulation of respiration but with the essential physiological structure of the nervous system. The reflex muscular effort and the respiratory rhythm having developed from the original mass movement are linked together. The phenomenon in ordinary

mammalian physiology which seems most closely allied is that described by Krogh & Lindhard [1913], who, in their classical paper, show that "at the commencement of heavy work...the rise in ventilation...is produced by irradiation from the motor cortex".

The cessation of the rhythmic movements

About the 50th day, one-third of the way through fœtal life, a great alteration takes place: the fœtus from being very active becomes inert and the phenomena which have been described are usually not visible. The essential nature of this change is a matter for future investigation: here it can only be said that the mechanism which has been elaborated is not abolished: it is only dormant. One way of revealing it is that of subjecting the fœtus to asphyxial conditions, as by pinching the umbilical cord for a short time.

The relation of the movements described in this paper to those observed by Snyder [1936] in rabbit fœtuses at term cannot at present be precisely stated, and depends upon the relative maturities of rabbit fœtuses at term (30 days) and 49 day sheep fœtuses. Anoxæmia appears to depress both. There is a similar difficulty in comparing our results with the instructive paper of Corey [1932].

Summary

1. The rhythmic trunk movements associated with ordinary respiration are developed between the 38th and 49th days of fœtal life in the sheep (gestation period about 157 days).

2. They are derived from a general mass movement of an extensor type by the dropping out of the movements of the head and limbs.

3. They cannot be elicited at this stage by asphyxial conditions of the blood.

4. Towards the 49th day their frequency becomes more rapid and they become more powerful as the result of muscular effort.

5. The above phenomenon seems to be of the same nature as the irradiation hyperpnœa of Krogh & Lindhard.

6. After the 50th day the rhythmic movements disappear as a spontaneous phenomenon but can be elicited by stoppage of the blood flow in the umbilical cord.

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