component characterizes all flecked animals, or whether there are other genetic factors that play a part in determining the size of this component.

The situation described here resembles the ocular albinism that occurs in man (*10*). This is a sex-linked abnormality. Affected males show the visual abnormalities that characterize full albinos, while the carrier females show a patchy distribution of retinal pigment and no visual defects. One could argue that if there were abnormal retinal patches in the females, these could be too small to be identifiable clinically, but it seems more reasonable to conclude that the females are like the flecked mice and have a completely normal visual system.

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References and Notes

1. R. W. Guillery, *Brain Res.* **14**, 739 (1969); R. D. Lund, *Science* **149**, 1506 (1965); *ibid.* **33**, 482 (1971); D. J. Creel, *Nature* **231**, 465 (1971); R. W. Guillery, C. Sitthi Amorn, B. B. Eighmy, *Science* **174**, 831 (1971).
2. R. W. Guillery and J. H. Kaas, *J. Comp. Neurol.* **143**, 73 (1971); D. H. Hubel and T. N. Wiesel, *J. Physiol. London* **218**, 33 (1971).
3. A. G. Searle, *Comparative Genetics of Coat Colour in Mammals* (Logos, London, 1968).
4. B. M. Cattanach, *Z. Verebungslehre* **92**, 164 (1961).
5. S. Ohno and B. M. Cattanach, *Cytogenetics* **1**, 129 (1962).
6. M. F. Lyon, *Nature* **190**, 372 (1961); *Biol. Rev.* **47**, 1 (1972).
7. M. S. Deol and W. K. Whitten, *Nature New Biol.* **238**, 159 (1972).
8. D. C. Pease, *Histological Techniques for Electron Microscopy* (Academic Press, New York, ed. 2, 1964).
9. Retinal pigmentation has been examined in flecked mice from a closely related stock; there was a slight excess of pigmented cells over unpigmented ones (*6*). This small difference should not affect our conclusions.
10. S. Duke-Elder, *System of Ophthalmology*, vol. 3, *Normal and Abnormal Development*; part 2, *Congenital Deformities* (Mosby, St. Louis, 1963).
11. This work was done while R.W.G. was a visiting Science Research Council Fellow in the anatomy department of University College, London. Two of us (R.W.G. and G.L.S.) thank Professor J. Z. Young and Dr. S. M. Zeki for creating the opportunity for us to work in the anatomy department. We thank Professor E. G. Gray for generously making his facilities available for this work, Mr. G. Haulgate for help with the photographic processing; and Miss S. Johnson for technical assistance. Supported by PHS grant R01 NS06662.

6 October 1972

Swallowing in Fetal Sheep

Abstract. *Swallowing was measured in fetal sheep by using electromagnetic flowmeter heads chronically implanted in the fetal esophagus. The fetus swallows 20 to 200 milliliters of amniotic fluid in two to seven discrete episodes per day. The episodes are 1 to 9 minutes in duration and occur at seemingly random intervals. Swallowing is influenced by the condition of the fetus and may be the first manifestation of eating and drinking behavior.*

It is well established that many mammalian species, including rats, guinea pigs, sheep, and humans, swallow in utero (*1, 2*). The only quantitative data on fetal swallowing, however, are estimates of volume swallowed per 24 hours by humans (*2*). Fetal swallowing activity may contribute to the control of amniotic fluid volume and may be the forerunner of adult eating and drinking behavior. Before the possible functional significance of fetal swallowing can be understood, the behavior itself must be studied in more detail. In this study swallowing was measured in fetal sheep by means of an electromagnetic flow transducer chronically implanted in the fetal esophagus. The method provides continual data over periods of weeks on the frequency of intrauterine swallowing and the volume of amniotic fluid swallowed at any given time.

Nine dated pregnant ewes in the last third of gestation were operated under sterile conditions. The general surgical procedure is as described in Dawes *et al.* (*3*). A midline abdominal incision was made to expose the uterus. The fetal head was palpated through the uterus and withdrawn through the abdominal incision. The uterus and fetal membranes were incised and the fetal head was delivered. Loss of amniotic fluid was minimized by clamping the uterus and membranes to the fetal neck skin. A cannulated electromagnetic flowmeter head (*4*) with an internal diameter of 3, 4, or 5 mm was inserted through a longitudinal incision into the fetal esophagus. The incision was sutured over the flowmeter cannula. A catheter was inserted into the carotid artery for sampling fetal blood and measuring blood pressure. A catheter was inserted into the fetal trachea for measuring tracheal pressure. Two catheters for injection of chemicals into and sampling from the amniotic fluid were sutured to the fetal head and snout. After implantation of all catheters the fetal head was replaced in the uterus and uterine and abdominal incisions were closed. The ewe was kept in a metabolism cage after surgery. The carotid arterial and tracheal catheters were connected to pressure transducers; the externalized lead from the esophageal flow transducer was connected to the flowmeter. The flowmeter provided a continuous measurement of esophageal flow with very low baseline drift (*5*). Volumes swallowed were obtained by integrating the flowmeter output over successive 1-minute periods. Records of flow rate, volume swallowed, and carotid and tracheal pressures were made continuously on a 24-hour basis.

Records of integrated esophageal flow, or volume swallowed, for one fetus are presented in Fig. 1. These records are characteristic of the swallowing activity of the sheep fetus during the last third of gestation. Over a 24-hour period the fetus swallows in discrete episodes or bouts. A bout consists of a period of swallowing during

Table 1. Average volumes swallowed per day by fetuses with electromagnetic flowmeter heads chronically implanted in the esophagus. Averages do not include volumes swallowed on the day of operation or the first postoperative day.

Age of fetus (days)	Internal diameter of flowmeter cannula (mm)	Volume swallowed per day (mean ± S.D.) (ml)	Number of bouts per day (mean ± S.D.)	Weight of fetus at delivery (kg)
109 to 123	3	126 ± 30 (9)*	2 ± 1	2.49
110 to 125	4	150 ± 68 (9)	3 ± 1	3.00
115 to 129	4	359 ± 147 (9)	5 ± 2	2.88
118 to 141	4	243 ± 86 (20)	4 ± 1	3.92
119 to 123	4	491 ± 0 (1)	9 ± 0	3.92
120 to 125	4	79 ± 51 (3)	1 ± 1	3.18
121 to 135	4	149 ± 60 (9)	2 ± 1	3.10
122 to 128	5	477 ± 203 (3)	6 ± 2	3.10
136 to 143	4	403 ± 207 (4)	5 ± 2	3.15

* The number of days from which the average was calculated is given in parentheses.

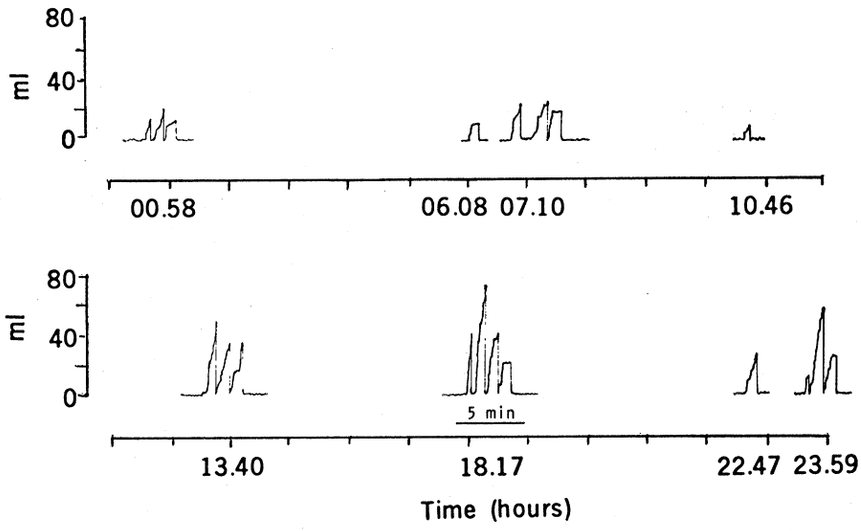

Fig. 1. Integrated records of swallowing bouts over 24 hours from a 125-day fetal sheep on the third postoperative day. The time at which swallowing occurred is indicated under each integrated record. The integrator automatically resets to zero every minute. The 24-hour total was 568 ml.

which 20 to 200 ml of amniotic fluid are consumed. The bouts are 1 to 9 minutes in duration, and two to seven bouts occur per day. The volumes swallowed per bout vary greatly for a given fetus on a given day, as seen in Fig. 1. In between the episodes of large volume swallowing, the fetus occasionally swallows smaller volumes (1 to 10 ml).

Fetal swallowing bouts similar to those in Fig. 1 were observed in nine fetuses, aged 109 to 143 days gestation, over a total of 103 days recording time. The swallowing bouts did not occur at predictable intervals, nor was an obvious pattern of swallowing established from day to day. However, not enough data are available for rigorous analysis of inter-bout intervals.

The average volume of amniotic fluid swallowed per day ranged from 79 to 491 ml in nine fetuses (Table 1). Similar variability in volumes swallowed have been reported among human fetuses, ranging from 200 to 760 ml/day (*2*, *6*). It is possible that the cannulated flowmeter heads used in this study do not completely occlude the esophagus of the fetal sheep; during swallowing some amniotic fluid may flow around the outside of the transducer. Therefore, volumes reported here may not represent total volumes swallowed.

Three conditions appeared to affect the daily volume swallowed. First, after operation 2 days of low-volume swallowing usually elapsed; on the third or fourth postoperative day the volume swallowed generally reached a peak for the preparation. Decreased swallowing after surgery is probably due in part to the healing of the esophageal incision. Second, in two ewes that went into labor at term, fetal swallowing decreased and then stopped 2 days before obvious signs of labor were detected. This is in contrast to suggestions that human fetuses swallow more fluid during labor (*6*, *7*). However, in both of the sheep preparations that went into term labor, chemicals had been injected into the amniotic fluid at various gestational ages. The possibility that decreased swallowing in these preparations was related to the injections cannot be excluded. Third, in deteriorating preparations swallowing stopped days before signs of fetal ill health were detected from changes in blood gas or *p*H values.

Through the use of electromagnetic flowmeter heads chronically implanted in the fetal esophagus, it has become apparent that the fetal sheep swallows large volumes of amniotic fluid at irregular intervals throughout the day. If it were possible to induce swallowing bouts artificially, substantial quantities of chemicals could conceivably be administered to the fetus via the amniotic fluid. At present it is not possible to state what determines the volume swallowed during a bout, the length of bouts, or the time between bouts. If fetal swallowing is related to adult feeding behavior, stomach emptying may influence the occurrence of swallowing episodes. Fetal micturition may also influence swallowing. The volume of urine produced by the fetal sheep aged 120 days to term ranges from 173 to 677 ml/day (*8*), similar to the range of volume of amniotic fluid swallowed. It is possible that changes in amniotic fluid composition following micturition are detected by the fetus and initiate swallowing bouts. It has been shown that the taste receptors of fetal sheep are functional for at least the last third of gestation (*9*); the change in amniotic fluid composition due to urination could be detected by the taste receptors.

During sleep humans swallow at irregular intervals in association with a change in sleep pattern (*10*) and, presumably, with the need to remove saliva. From about 115 days the sheep fetus produces a thick mucoid oral secretion, and irregular outpourings of tracheal fluid also occur (*11*). However, the fetal mouth and pharynx are always fluid-filled. It is not yet clear, therefore, whether fetal swallowing is initiated by a change in the composition of this fluid, by accumulation of fluid in the mouth, by factors such as stomach emptying or urination, or by the fetal neural analog of thirst.

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References and Notes

1. R. Lev and D. Orlic, *Science* **177**, 522 (1972); R. F. Becker, W. F. Windle, E. E. Barth, M. D. Schulz, *Surg. Gynecol. Obstet.* **70**, 603 (1940); D. L. Duncan and A. T. Phillipson, *J. Exp. Biol.* **28**, 32 (1951).
2. J. A. Pritchard, *J. Obstet. Gynecol.* **25**, 289 (1965).
3. G. S. Dawes, H. E. Fox, B. M. Leduc, G. C. Liggins, R. T. Richards, *J. Physiol.* **220**, 119 (1972).
4. D. M. Clark and D. G. Wyatt, *Med. Biol. Eng.* **7**, 185 (1969).
5. D. G. Wyatt, *J. Physiol.* **173**, 8P (1964).
6. D. Gitlin, J. Kumate, C. Morales, L. Noriega, N. Arévalo, *Amer. J. Obstet. Gynecol.* **113**, 632 (1972).
7. L. A. Hamilton and R. E. Behrman, *ibid.* **112**, 834 (1972).
8. D. P. Alexander, D. A. Nixon, W. F. Widdas, F. X. Wohlzogen, *J. Physiol.* **140**, 14 (1958); J. H. G. Rankin, E. L. Gresham, F. C. Battaglia, E. L. Makowski, G. Meschia, *J. Appl. Physiol.* **32**, 129 (1972).
9. R. M. Bradley and C. M. Mistretta, *J. Physiol.* **218**, 104P (1971); in *Oral Physiology*, N. Emmelin and Y. Zotterman, Eds. (Pergamon, Oxford, 1972), p. 239.
10. C. S. C. Lear, J. B. Flanagan, C. F. A. Moorrees, *Arch. Oral Biol.* **10**, 83 (1965).
11. G. S. Dawes, in *Transactions of the Barcroft Centenary Symposium on Fetal and Neonatal Physiology* (Cambridge Univ. Press, Cambridge, in press).
12. This work was done at the Nuffield Institute for Medical Research, University of Oxford, Headington, Oxford, England. We thank Dr. G. S. Dawes and Dr. J. Robinson for advice on the research and Dr. K. Boddy and Dr. C. P. Gibbs for frequent help and encouragement. We acknowledge financial support from the Medical Research Council.

18 December 1972