CONFERENCE REPORT

Amniotic fluid dynamics

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Abstract. Amniotic fluid was once considered to be a stagnant pool, approximately circulating with a turnover time of one day. Adequate amniotic fluid volume is maintained by a balance of fetal fluid production (lung liquid and urine) and resorption (swallowing and intramembranous flow). Even though different hypotheses have been advanced on the mechanisms regulating this turnover, the inflow and outflow mechanism that keeps amniotic fluid volume within the normal range is not entirely clear. Regulatory mechanisms act at three levels: placental control of water and solute transfer; regulation of inflows and outflows from the fetus; and, maternal effect on fetal fluid balance. Amniotic fluid is 98-99% water. The chemical composition of its substances varies with gestational age. When fetal urine begins to enter the amniotic sac, amniotic osmolarity decreases slightly compared with fetal blood. After keratinization of the fetal skin, amniotic fluid osmolarity decreases further with advancing gestational age. The low amniotic fluid osmolarity, which is produced by the inflow of markedly hypotonic fetal urine, provides a large potential osmotic force for the outward flow of water across the intramembranous and transmembranous pathways. Within certain limits, amniotic fluid mirrors the metabolic status of the fetoplacental unit; for that reason, a study of its components and their respective variations in the different weeks of pregnancy provides useful indications, both for a correct assessment of fetal maturation and for an evaluation of kidney function parameters and placental insufficiency.

Key words: Amniotic fluid, physiology, regulatory mechanisms

Amniotic fluid physiology

About 4 liters of water accumulate within intrauterine compartments during the 40-week period of human gestation, with 2800 ml in the fetus, 400 ml in the placenta, and 800 ml in the amniotic fluid. At the beginning of pregnancy, amniotic fluid volume (AFV) is a multiple of fetal volume. The two volumes become equal soon after the 20th week, but by the 30th week AVF is about half the fetal volume and at term it is about a quarter of fetal volume. In the last trimester, near term, there are net increases of about 30 to 40 ml per day. Such daily net increases in intrauterine fluid exceed the amount that could originate from any intrauterine or fetal metabolic source, and thus must in large part be derived by transfer from the maternal compartment. Human placental tissue, a multicellular tissue layer with large extracellular spaces, reflects the physicochemical properties of a membrane system with significant porosity.

In normal pregnancies, a wide volume range is seen, particularly during the second half of gestation. The rate of change in AVF is a strong function of gestational age. There is a progressive AFV increase from 30 ml at 10 weeks' gestation to 190 ml at 16 weeks and to a mean of 780 ml at 32-35 weeks, after which a decrease occurs. The decrease in post-term pregnancies has been found to be as high as 150 ml/week from 38 to 43 weeks (1). Although the basic mechanisms that produce these AVF changes throughout gestation are unclear, it is important to note that, when expressed as a percentage, the rate of change decreases monotonically throughout the fetal period. Thus, the late decrease in AVF represents a natural progression rather than an aberration.

AVF is the sum of the inflows and outflows in the amniotic space. Thus, knowledge of the pathways for amniotic fluid movements is a prerequisite for understanding volume regulatory mechanisms (2). In early gestation, significant amounts of amniotic fluid are present before the establishment of fetal micturition or deglutition. Although the formation of amniotic fluid at this early stage is virtually unexplored, the most likely mechanism is an active transport of solute by the amnion into the amniotic space, with water moving passively down the chemical potential gradient. Much more is known about the pathways involved in the regulation of AVF during the second half of gestation after the fetal skin keratinizes. The excretion of fetal urine and the swallowing of amniotic fluid by the fetus are the two major pathways for the formation and clearance, respectively, of amniotic fluid.

1. Fetal urine is a major source of amniotic fluid in the second half of pregnancy. Urine first enters the amniotic space at 8-11 weeks' gestation, but the urine production rate shows a steady increase throughout the last half of gestation (3). Urine production per kilogram of body weight increases from approximately 110/ml/kg every 24 hours at 25 weeks to approximately 190 ml/kg every 24 hours at 39 weeks (4). At term, the current best estimate of fetal urine flow rate may average 700-900 ml/day.
2. The fetus begins swallowing at the same gestational age when urine first enters the amniotic space, that is around 8-11 weeks. It is estimated that the volume of amniotic fluid swallowed in late gestation averages 210-760 ml/day (5), and that this process primarily occurs during episodes of fetal breathing activity. These daily volumes do not include the amount of tracheal fluid from the lungs that is swallowed before it enters the amniotic space. Fetal swallowing plays an important role in determining AFV during the last half of gestation. In their study, Scott and Wilson (6) reviewed 169 cases of polyhydramnios; excess AVF was attributed to a disturbance in the fetal swallowing mechanism in 54 of them (32%). Their findings confirmed those of a more extensive review of 1,745 patients with polyhydramnios, which showed an 18% rate of swallowing disturbances (7).
3. The secretion of large volumes of fluid each day by the fetal lungs is now well established, so that the fetal lungs are the second major source of amniotic fluid during the second half of gestation. Studies in near-term fetal sheep have shown that there is an outflow from the lungs of 200-400 ml/day (8) and that this flow corresponding to 10% body weight/day is mediated by an active transport of chloride ions across the epithelial lining of the developing lung. Proof of this is that experimental techniques of intrauterine ligature of the fetal trachea cause expansion of the fetal lung. This corroborates the evidence of a relatively large column of fluid flowing out of the lung of the human fetus during normal pregnancy, even though its amount cannot be quantified.
4. As a further pathway, it has been discovered more recently (9) that rapid movements of both water and solute occur between amniotic fluid and fetal blood within the placenta and membranes; this is referred to as the intramembranous pathway. Movement of water and solute between amniotic fluid and maternal blood within the wall of the uterus is an exchange through the transmembranous pathway. The inward transfer of solute across the amnion with water following passively is the most likely source of amniotic fluid very early in gestation. Finally, amniotic fluid may be secreted by the fetal oral-nasal cavities, which contribute to AVF.
5. Finally, part of AVF may be derived from water transport across the highly permeable skin of the fetus during the first half of gestation, at least until keratinization of the skin occurs around 22-25 weeks. There is ample evidence that the rate of water metabolism and transepidermal water loss is greater in premature newborns than in full-term infants (10).

Amniotic fluid was once considered to be a stagnant pool, approximately circulating with a turnover time of one day. Even though different hypotheses have been advanced on the mechanisms regulating this turnover, the inflow and outflow mechanism that keeps amniotic fluid volume within the normal range is not entirely clear. Regulatory mechanisms act at three levels:

- Placental control of water and solute transfer.
- Regulation of inflows and outflows from the fetus: fetal urine flow and composition are modulated by arginine, vasopressin, aldosterone, angiotensin II, and atrial natriuretic peptide, in much the same way as they in adults. The mechanisms regulating fetal swallowing are less known.
- Maternal effect on fetal fluid balance: there is a strong relationship between maternal plasma volume expansion during pregnancy and AVF, so that subnormal plasma volume expansion is associated with oligohydramnios and elevated plasma volume with hydramnios. Kilpatrick et al. (11) reported that ingestion of 2 liters of water in women with a low amniotic fluid index (AFI) resulted in a significant 31% AFI increase.

Amniotic fluid is 98-99% water. The chemical composition of its substances varies with gestational age; up to around the 20th week, it reflects that of fetal extracellular fluid, because the skin of the fetus is not major obstacle to the free exchange of substances. When fetal urine begins to enter the amniotic sac, amniotic osmolarity decreases slightly compared with fetal blood. After keratinization of the fetal skin, amniotic fluid osmolarity decreases further with advancing gestational age, reaching values of 250-260 mOsm/kg water near term. The low amniotic fluid osmolarity, which is produced by the inflow of markedly hypotonic fetal urine, provides a large potential osmotic force for the outward flow of water across the intramembranous and transmembranous pathways. Within certain limits, amniotic fluid mirrors the metabolic status of the fetoplacental unit; for that reason, a study of its components and their respective variations in the different weeks of pregnancy provides useful indications, both for a correct assessment of fetal maturation and for an evaluation of kidney function parameters and placental insufficiency.

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