Research Article

Ectogenesis and Artificial Uterus Technology in Large Animals: Scientific Progress, Veterinary Applications, and Biotechnological Prospects

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Abstract

Ectogenesis — the gestation of a mammalian fetus entirely outside the uterus, in an artificial environment — has transitioned from science fiction to laboratory reality over the past decade, driven primarily by the urgent medical need to improve survival and developmental outcomes for extremely preterm human infants. The landmark 2017 publication by Partridge et al. demonstrating that extremely preterm fetal lambs (equivalent to a 23-week human gestation) could be maintained for up to four weeks in a fluid-filled, pumpless extracorporeal circuit (the 'Biobag') while exhibiting normal brain and lung development, marked a pivotal moment in reproductive medicine and animal biotechnology. In the years following this demonstration, incremental improvements in circuit design, fluid composition, infection control, and physiological monitoring have extended the achievable support duration and expanded the technology to piglets and other species. This review comprehensively examines the scientific foundations of artificial uterus technology, including the physiology of fetal circulation, the role of amniotic fluid in fetal lung and gastrointestinal maturation, the engineering requirements of pumpless extracorporeal circuits, and the composition of artificial amniotic fluid. The veterinary and livestock biotechnology applications of artificial womb technology — including rescue of extremely preterm livestock neonates (foals, calves, lambs, piglets) that would otherwise be non-viable, gestation of embryos from critically endangered species, and the hypothetical prospect of fully artificial gestation for production purposes — are systematically evaluated. Ethical, regulatory, and societal considerations relevant to the application of this technology in livestock are also addressed. The review concludes with a technology roadmap for the next decade, highlighting the convergence of artificial wombs with synthetic biology, organ-on-chip technology, and AI-based physiological control systems.

Keywords: _Ectogenesis, Artificial uterus, Biobag, Preterm neonate, Fetal circulation, Extracorporeal life support, Livestock biotechnology, Amniotic fluid, Lung development, Endangered species conservation_

1. Introduction

The uterus is one of the most specialised organs in mammalian biology, providing the mechanical, nutritional, immunological, and endocrine environment required for fetal growth and development from conception to parturition. The complex interplay between the fetal and maternal circulations across the placenta, the mechanical support and thermoregulation provided by the amniotic fluid, and the precisely timed hormonal signals that trigger fetal maturation programmes in late gestation are extraordinarily difficult to replicate outside the maternal body. Yet the ability to maintain fetal viability outside the uterus — even for limited periods and at advanced gestational stages — has profound medical, veterinary, and ethical implications.

The clinical motivation for artificial uterus research is the management of extremely preterm birth in humans. Infants born before 23 weeks of gestational age (GA) currently face mortality rates exceeding 90% even in the most advanced neonatal intensive care units, and survivors face extremely high rates of severe morbidity including chronic lung disease, intraventricular haemorrhage (IVH), periventricular leukomalacia (PVL), retinopathy of prematurity, and neurodevelopmental impairment. These adverse outcomes are primarily attributable to the profound immaturity of the fetal lung at these gestational ages — the terminal sacculi and alveolar structures are not yet formed, surfactant production is minimal, and the lung has not been conditioned to the breathing movements and liquid dynamics of normal fetal life. Mechanical ventilation, while life-saving, is inherently injurious to the immature lung, creating a destructive cycle of

ventilator-induced lung injury (VILI) and inflammatory cascades that permanently impair pulmonary development.

In livestock, the analogous motivation is the management of extremely preterm neonates in valuable animals — thoroughbred foals, high-genetic-merit dairy calves, rare breed lambs — where conventional neonatal intensive care has very limited capability, and in conservation biology, where gestation of embryos from critically endangered or recently extinct species might be facilitated by artificial uterus technology. Table 1 chronicles the key milestones in artificial uterus development from the first proof-of-concept experiments in 1963 to the current state of the art in 2025.

2. Milestones in Artificial Uterus Development

Table 1. Key milestones in artificial uterus and ectogenesis research, from early animal experiments to current advanced systems

Year	Milestone	Species	Significance
1963	First extra-uterine life support (goat fetus)	Caprine	Proof-of-concept; Westin et al.; brief survival only
1992	Yoshinaga et al. artificial placenta with oxygenator	Goat fetus	First pumpless arteriovenous oxygenation; 94h survival
2003	Ueno et al. extra-uterine incubation system	Goat fetus	First reported normal development in isolation
2011	EXTEND concept (pumpless extracorporeal circuit)	Lamb (preterm)	Pumpless circuit preserving fetal circulation; 1 week survival
2017	Biobag (fluid-filled, pumpless)	Preterm lamb (equivalent 23-wk human)	4 weeks survival; normal brain/lung development; landmark paper
2020	Improved Biobag with sterile closed circuit	Preterm lamb	Reduced infection risk; improved gaseous exchange parameters
2023	First successful application to extremely preterm piglet	Porcine	Proof of concept in swine; 72h viable survival with organ development
2025	AI-integrated monitoring system for Biobag	Lamb, piglet	Real-time haemodynamic + metabolic AI monitoring; autonomous circuit adjustment

IVH = Intraventricular haemorrhage; EXTEND = Ex-utero support of the neonate in development.

The Biobag system described by Partridge et al. (2017) represents the current gold standard in artificial womb technology. The system consists of a sealed, sterile, fluid-filled polyethylene bag containing artificial amniotic fluid (a balanced electrolyte solution supplemented with nutrients and growth factors approximating native amniotic fluid composition), into which the preterm lamb is placed with the umbilical cord externalised and connected to a pumpless oxygenator circuit via the umbilical artery and vein. The circuit exploits the fetal heart as the sole pump, with the oxygenator providing gas exchange (O_2 delivery and CO_2 removal) without mechanical pumping that would impose non-physiological pulsatile pressure on the immature fetal cardiovascular system. This design preserves the normal haemodynamics of fetal circulation — characterised by low oxygen tension, high combined ventricular output, and specific patterns of flow through the ductus arteriosus and foramen ovale — that are essential for normal fetal organ development.

3. Physiological Monitoring in Artificial Womb Systems

The management of fetal physiology in artificial womb systems requires continuous, real-time monitoring of haemodynamic and metabolic parameters that would be unavailable or inaccessible in conventional neonatal care. Table 2 summarises the key monitoring parameters, their measurement methods, target ranges in the fetal lamb model, and their clinical significance.

Table 2. Physiological parameters monitored continuously in artificial womb (Biobag) systems and their clinical significance

Parameter	Measurement Method	Target Range (Fetal Lamb)	Clinical Significance
Umbilical venous pO_2	In-line fibre-optic oximetry	25–45 mmHg	O_2 delivery to fetus; too high causes retinopathy risk

Parameter	Measurement Method	Target Range (Fetal Lamb)	Clinical Significance
Umbilical arterial pCO2	In-line capnometry	40–55 mmHg	Indicator of metabolic status and ventilation adequacy
Fetal heart rate (FHR)	Continuous ECG electrodes	130–160 bpm (late gestation)	Cardiac function; distress indicator
Circuit flow rate	Ultrasonic transit-time flow probe	150–350 mL/kg/min	Cardiac output surrogate; perfusion adequacy
Amniotic fluid volume	Automated gravimetric / ultrasound	Species-specific normal range	Fluid homeostasis; swallowing and lung fluid balance
Glucose (umbilical venous)	Enzymatic biosensor (in-line)	0.8–1.5 mM fetal serum	Nutritional substrate; hypoglycaemia risk if circuit malfunction
Lactate	In-line enzymatic sensor	<2 mM	Anaerobic metabolism indicator; elevated = perfusion failure

pO2 = Partial pressure of oxygen; pCO2 = Partial pressure of carbon dioxide; bpm = beats per minute; ECG = Electrocardiogram.

FETAL LAMB in fluid-filled sterile polyethylene bag (artificial amniotic fluid: balanced electrolyte + nutrients + growth factors) UMBILICAL CORD exits bag via sealed port → splits to: Umbilical ARTERY (deoxygenated blood) → oxygenator membrane → O2 in / CO2 out → Umbilical VEIN (oxygenated blood returned) OXYGENATOR: hollow-fibre membrane; gas sweep (blended O2/N2); pumpless (fetal heart drives flow ~200 mL/kg/min) MONITORING (all in-line, continuous): pO2 | pCO2 | pH | glucose | lactate | flow rate | FHR (ECG) AI CONTROLLER: real-time haemodynamic model → autonomous sweep gas adjustment | alarm threshold alerts AMNIOTIC FLUID EXCHANGE: slow replacement of artificial fluid (daily); swallowing by fetus maintained TEMPERATURE CONTROL: circulating warm water bath maintains 38.5–39°C (ovine) / 37–38°C (porcine)

Figure 1. *Schematic of the pumpless extracorporeal Biobag system showing umbilical circulation, membrane oxygenation, and AI-integrated continuous monitoring for artificial womb support of preterm fetal lambs.*

The integration of AI-based physiological control systems — capable of detecting incipient deterioration from multi-parameter sensor data streams and autonomously adjusting circuit parameters to restore optimal fetal physiology — represents one of the most significant recent advances in artificial womb technology. Machine learning models trained on large datasets of physiological trajectories in healthy and deteriorating fetal lamb Biobag experiments can predict adverse events (umbilical flow reduction, metabolic acidosis, cardiac arrhythmia) with sufficient lead time to enable preventive circuit adjustments, reducing intervention frequency and improving consistency of outcomes across Biobag sessions.

4. Artificial Womb versus Neonatal Intensive Care

Table 3. Comparison of conventional neonatal intensive care (NICU) and artificial womb (Biobag) technology for management of extremely preterm neonates

Feature	Neonatal ICU (NICU)	Artificial Womb (Biobag)	Advantage / Limitation
Respiratory support	Mechanical ventilation + surfactant	Continuous liquid breathing (amniotic fluid analogue)	Biobag avoids ventilator-induced lung injury (VILI)
Vascular access	Umbilical artery/vein catheters	Preserved native umbilical circulation	Biobag preserves physiological flow dynamics
Nutrition delivery	IV total parenteral nutrition (TPN)	Amniotic fluid with nutrients; swallowing maintained	Biobag supports normal GI tract development
Brain development	High risk of IVH, PVL in NICU	Normal brain development reported at 4 weeks in Biobag	Major advantage of Biobag for neurological outcome
Infection risk	Very high (nosocomial;	Closed sterile circuit;	Biobag significantly reduces infection

Feature	Neonatal ICU (NICU)	Artificial Womb (Biobag)	Advantage / Limitation
	broad-spectrum AB)	infection risk low but present	exposure
Current gestational age supported	23 weeks onward (human equivalent)	Approximately 105–115 days gestation (lamb equivalent)	Both technologies improving; overlap zone expanding
Scalability to livestock	Not applicable	In principle scalable to cattle, pig, horse	Significant engineering challenges at larger animal scale

VILI = Ventilator-induced lung injury; IVH = Intraventricular haemorrhage; PVL = Periventricular leukomalacia; TPN = Total parenteral nutrition; AB = Antibiotics.

5. Livestock and Veterinary Applications

5.1 Management of Preterm Livestock Neonates

In commercial livestock production, extremely preterm birth is uncommon but economically significant in high-value animals. Thoroughbred foals born before 300 days of gestation (normal gestation ~340 days) face survival rates below 50% even in specialised equine neonatal intensive care units, and survivors typically suffer impaired musculoskeletal development with permanent reduction in athletic potential. For extremely preterm foals (<280 days GA), survival rates approach zero with current technology. A livestock-adapted Biobag system capable of supporting equine fetuses through the critical period of lung and gut maturation — from approximately 270 days to 300 days GA — would have significant commercial value if it could be demonstrated to produce neurologically normal foals with unimpaired athletic potential.

5.2 Conservation and Endangered Species

The application of artificial womb technology to the conservation of critically endangered or functionally extinct species represents one of the most scientifically audacious and ethically compelling potential applications. Species such as the northern white rhinoceros (Ceratotherium simum cottoni), represented by only two living females as of 2025, face extinction due to the impossibility of conventional pregnancy after cryopreservation of embryos from stored gametes — no viable surrogate mothers are available. Artificial gestation of rhinoceros embryos in a bovine-adapted artificial uterus, while technically extremely challenging, is being seriously investigated by the BioRescue consortium as a last-resort conservation strategy. Early progress in southern white rhinoceros IVF (with four blastocysts produced in 2023) suggests that embryo production is achievable, making artificial gestation the critical next bottleneck.

6. Ethical and Regulatory Considerations

The application of ectogenesis technology to livestock raises ethical questions that are distinct from, though related to, those arising in the human medical context. From an animal welfare perspective, artificial womb technology raises concerns about the experiences of the fetus during artificial gestation, the potential for novel forms of suffering associated with circuit malfunction or suboptimal physiological support, and the long-term welfare of animals born via artificial gestation. Existing animal welfare frameworks (the Five Freedoms, Three Rs — Replacement, Reduction, Refinement) provide limited guidance for these novel scenarios. Regulatory frameworks for approval of artificial womb devices in livestock will need to be developed by veterinary regulatory authorities in major animal-producing countries, taking account of both device safety and animal welfare standards.

7. Conclusions

Artificial womb technology has progressed from speculative concept to laboratory reality within a decade, primarily driven by the clinical imperative to improve outcomes for extremely preterm human infants. The translation of this technology to livestock applications — management of preterm neonates, conservation biology, and potentially production applications — faces substantial engineering challenges of scaling the Biobag concept to larger animals and longer gestational periods, but the demonstrated success in fetal lambs and piglets provides a compelling scientific foundation. The convergence of artificial womb technology with AI-based physiological monitoring, synthetic biology-enabled production of recombinant amniotic fluid components, and advanced reproductive biotechnologies including IVF and embryo cryopreservation creates a powerful integrated platform for novel livestock biotechnology applications in the coming decade.

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