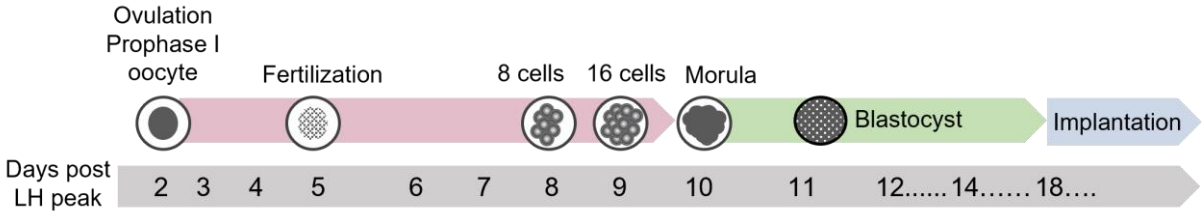
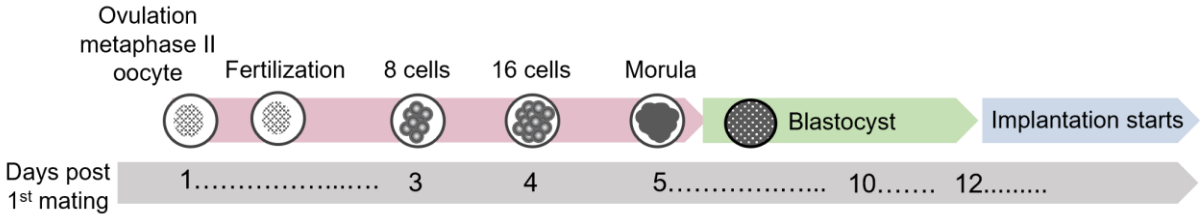
**Supplementary Figure 1. Kinetics of embryo development.** Timings are approximate estimates of *in vivo* events. Development stages at different times will vary by embryo and individual dam. Pink arrows denote events occurring in the oviduct; green and blue arrows denote events in the uterine horns. LH, luteinizing hormone.

**a) Dog** (1-5)




**b) Cat** (6, 7)



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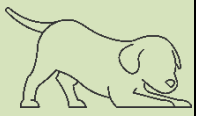
**Supplementary Table 1. Overview of organogenesis and early development in dogs for selected organs.** D, day; Mth, month; Wk, week; Yr, year.

| Period | Immune system | Cardiovascular & musculoskeletal system | Reproductive organs | Pituitary and adrenal glands and pancreas | Gut | Brain, neuroendocrine system, vision |
|---|---|---|---|---|---|---|
| **Embryo**<br>**Day 19–35**  | • D27–28: Primordia of spleen and thymus evident (1) | • D21–22: Primordial heart apparent (2)<br>• D21–24: Heart beat first visible (3)<br>• D22–25: Early development of limbs (2)<br>• D28:First ossification of skeleton observed (4) | • D22: Primordial germ cells detected in gonadal ridge (5)<br>• D22: Global DNA demethylation occurs in the male canine gonadal ridge (6)<br>• D21–25: Gonads remain undifferentiated (4) | • D25:Adeno-hypophysis first identifiable (7)<br>• D27: Primordial adrenal glands appear (7)<br>• D30: Pancreatic cells first detected – insulin +ve β-cells and α-cells (7) | • D22–25: Primitive gut established (2) | • D22–25: Brain vesicles (forebrain, midbrain and hind brain) have formed (2)<br>• D25–28: Retinal precursor formed (8)<br>• D29–32: Primitive brain still developing (2) |
| **Fetus**<br>**Day 35 to birth**  | • D35–40: Thymus actively lymphopoietic (1)<br>• D45: Thymus microenvironment complete (1, 9)<br>• D45–52: Lymphocytes infiltrate lymph nodes (1)<br>• D45: Lymphocytes respond to mitogen (1, 9)<br>• D50: Thymocytes can respond to mitogen (1, 9)<br>• D45–52: Abundant hemopoietic stem cells in bone marrow (1)<br>• D45–55: Peyers patches present in small intestine (1) | • D35: Complete cardiovascular system apparent (2)<br>• D57: Last bones ossify (4) | • D35–40: Sex differentiation begins (5)<br>• Prespermatogonia present before birth (6) | • D38: Pituitary gland has same morphology as in adult dog (10) | • D44+: Differentiation of layers in gut wall detectable by ultrasound (11) | • D35: Metencephalon, optical source bridge and cerebellum forming (2)<br>• D35: Myelencephalon starting to form oblong medulla (2) |

## Supplementary Table 1 continued

| | | | | | | |
|---|---|---|---|---|---|---|
| **Birth to 8 weeks**<br><br>Timings relative to birth<br>  | • At birth: Blood concentration of maternally derived antibodies close to zero (1, 12)<br>• At birth: functionally mature Peyer's patches (1)<br>• At birth a functional B and T cell system present (1)<br>• Day 1: Immunocompetent (post vaccination kinetics of antibodies similar to older puppies) (13)<br>• Days 0–21: Marked changes in proportions of different lymphocyte subsets (14) (12) | • D18–21: Walking commences and is co-ordinated by D28 (15)<br>• Wk 4–6: Pronounced change from developmental to adult isoforms of myosin heavy chain in skeletal muscles (16) | • At birth: Ovary contains oogonia, but no follicles (17)<br>• Wk 2–3: First primordial follicles (17)<br>• Mth2: Germinal cells degenerated (female) (17)<br>• Wk 1: Uterine adenogenesis underway and prepubertal glandular proliferation complete by Wk6 (18) | • At birth: Adrenal capsule elements present but poorly demarcated (19)<br>• Wk8: global organization of pancreatic tissue mature (20)<br>• Wk8: Ratio of α:β cells is still less than in the adult (20)<br>• By Mth1: in adrenal gland demarcation between capsule and cortex evident and 3 cortical zones well defined (19) | • 16–24 hours: Gut closes to absorption of immunoglobulins (21)<br>• D1: GI tract colonized–aerotolerant bacteria dominant. Anaerobic bacteria subsequently increase in number and proportion (22)<br>• Wk 8: Microbiome changes significantly with age at least to Wk8 (23, 24) | • D16–36: Photoreceptors develop (8)<br>• Birth–Wk3: First cycle of postnatal myelinization of spinal cord (26)<br>• Wk4: Autonomic thermoregulation (15)<br>• By Wk4–5: Conditioned reflexes of vision and audition (26)<br>• By Wk6: Second cycle of postnatal myelinization (26)<br>• By Wk6: Neuronal development of sensory, motor, visual and auditory cortex relatively mature (26)<br>• Wk6: Brainstem and cerebellum have adult appearances (25)<br>• Wk8: Retina is mature (8) |
| **Post weaning**<br><br>Timings relative to birth<br>  | • Beyond Yr1: Proportion of lymphocyte populations continue to change (1)<br>• Mth2–3: Serum IgM levels attain adult levels (1)<br>• Mth6–9: Serum IgG levels approximate to adult levels (1)<br>• Mth12: Serum IgA levels attain adult levels (1)<br>• By Yr1: Serum immunoglobulin levels believed to reach adult values (12)<br>• Mth6–23: Thymus involution (12) | • By Mth2: Maturation of skeletal muscle fibres in terms of transition to adult myosin heavy chain isoforms nearly complete (16)<br>• Up to Yr2: Growth plates continue to close until up to 24 months (27) | • Mth4: Primary or early preantral follicles (6)<br>• Mth4 to Mth 5–6: Early antral follicles observed (6)<br>• Mth 6 onwards: Advanced antral follicles (6)<br>• ~Mth7: Spermatogenesis starts (~60-day cycles) (5) | • Up to Yr1: Marked morphological changes continue in adrenal gland (19)<br>• Age-related changes in chymotrypsin and amylase activity of pancreatic tissue apparent until adulthood (28) | • By Wk6: Greatest changes in gut microbiome have occurred (24) but changes still evident during Yr1 {You, 2021 #559}<br>• Gastric pepsin activity increases between D63 and adulthood (28)<br>• Apparent macronutrient digestibility increases until the end of growth (30) | • Learned responses such as delayed response develop after Wk8 (26)<br>• Wk 16: Corpus callosum and cerebrum have adult appearances (25)<br>• Neocortex myelinization continues until ~Mth9 (26) |

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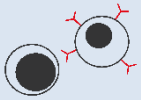
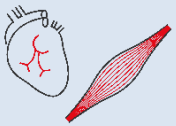
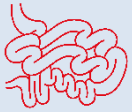
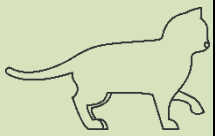
**Supplementary Table 2. Overview of organogenesis and early development in cats for selected organs.** D, day; Mth, month; Wk, week; Yr, year.

| Period  | Immune system  | Cardiovascular & musculoskeletal system  | Reproductive organs  | Pituitary and adrenal glands and pancreas  | Gut  | Brain, neuroendocrine system, vision  |
|---|---|---|---|---|---|---|
| **Embryo Day 19–35**  | • D25: Lymphocytes in circulation (1)<br>• D25: Lymphocytes in circulation (1)<br>• D28–32: Lymphocytes scattered in developing lymph nodes (2)<br>• D32–38: First lymphoblasts in thymus (2) | • D18–19: Limb buds appear (2)<br>• D21: Primordial heart apparent (3)<br>• D22–25: Early development of limbs (3)<br>• D25–28: Lower limb starts perichondral ossification (2) | • D19–21: Genital ridge ventromedial of mesonephros (2)<br>• By Day 32: Testes and ovary are differentiated (2) | • D19–21: Pancreas primordia distinct (2)<br>• D23–25: Adrenal glands are differentiating (2)<br>• (2)D25–28: Adrenals produce corticoids (2)<br>• D25–28: Pancreas differentiates (2)<br>• D28–32: Adrenal cortex and medulla separated (2)<br>• D32–38: First pancreas islets (2) | • 16 hours: Immunoglobulin absorption stops (1)<br>• D22–25: Primitive gut established (3)<br>• D25–28: Gastric glands and intestinal villi form (2) | • D22–25: Brain vesicles (forebrain, midbrain and hind brain) formed (3) |
| **Fetus Day 35 to birth**  | | • D32: Complete cardiovascular system apparent (3)<br>• D34–38: skeletal muscle spindles have single primary myotubes with simple innervation (4) | • D38–44: Genitals are differentiated (2) | | | |

## Supplementary Table 2 continued

| | | | | | | |
|---|---|---|---|---|---|---|
| **Birth to 8 weeks**<br><br>Timings relative to birth<br><br>  | • At birth: Blood concentration of maternally derived antibodies close to zero (1, 5)<br>• At birth: Inability to mount substantial immune response to antigen (6)<br>• Wk6–12: Immunocompetence considered to be achieved but depends upon colostrum immunoglobulins ingested (1)<br>• D1 to at least Mth 3: proportions of some lymphocyte subsets change in serum, thymus and lymph nodes (6) | • By birth: Assembly of extra- and intrafusal skeletal muscle fibres (4)<br>• ~D31: Adequate standing and imperfect walking (7)<br>• ~D44: Normal walking and running (7) | • ~Mth 1: First primordial follicles appear (8) | | | • Birth–Mth3: All neurological functions mature progressively (7)<br>• D8–13: Spatial localization of auditory stimuli starts and complete by D12–20 (7)<br>• D10–15: Interactions with siblings, mother and/or objects, and play start (7)<br>• Day 26: Visual orienting observed (7)<br>• D30: Volumes of the neocortex, caudate nucleus, thalamus and substantia nigra are within adult ranges (9, 10)<br>• D47–83: Binocular coordination complete (7)<br>• D60: Volume of the red nucleus is within adult range (9)<br>• D70: Peak synaptic density in the visual cortex followed by significant decline (11) |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Post weaning**<br><br>Timings relative to birth<br>  | • Lymphocyte populations continue to change (6)<br>• Mth5–9: Secretory IgA from bile reaches adult levels (12)<br>• Mth 5+: Serum IgA reaches adult levels after Mth5 (13)<br>• Mth6–8: thymus starts to involute (1) | | | | • By Wk 30–42: Gut microbiome has stabilized (14) | • Mth6: Volume of telencephalic white matter is close to adult volume (10)<br>• Mth3: Cerebral protein synthesis peaks in some brain regions (15)<br>• Mth6: local cerebral metabolic rate for glucose stabilizes to adult level (16) |

**References Supplementary Table 2**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