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メタデータ	言語: English 出版者: 日本DOHaD研究会 公開日: 2019-01-31 キーワード (Ja): キーワード (En): 作成者: Nishimura, Hiroko, Yaoita, Eishin, Sequeira-Lopez, Maria Luisa S., Gomez R., Ariel メールアドレス: 所属:
URL	<a href="http://hdl.handle.net/10271/00003493">http://hdl.handle.net/10271/00003493</a>

## Delayed body growth and structural defects originate in mechanical stress imposed during early embryonic life

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### [Background and Objectives]

Stress and insufficient nutrition in fetal life impose a risk of low birth weight (LBW) and increased vulnerability to chronic childhood and adult diseases. Using a unique avian model, we reported previously that reduced nutrition (protein) caused reduced hatching rate, structural abnormality, LBW, and, after maturation, a low number of nephrons, enhanced glomerular apoptosis, and glomerular mesangial lesions partly resembling glomerulosclerosis. In the present study, we aimed to determine whether delayed body growth and structural defects originate in mechanical stress or in reduced nutrition imposed on the embryo during the early period of development.

### [Methods]

Before the start of incubation (37.6°C, 70% humidity), using a sterile technique, 10% of the egg white (92% of solid constituents is protein) was withdrawn (EwW) from eggs of Japanese quail, *Coturnix japonica* (GQF MFG Co.; Savannah, GA) by gentle suction (a G18 blunt needle) through a 4 x 5 mm window. Control (CT), sham CT (opening a window only), EwW, and EwW-R (withdrawn egg white was immediately returned to the egg) groups were examined for body growth (body weight, BW, and body length, BL), and the morphology and  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA) expressions of the kidney.

### [Results]

We found: On embryonic day 8 (E8), 11% (EwW) and 38% (EwW-R) of embryos showed structural defects and/or early death, whereas at E15-16 (hatch, E17), 44% (EwW) and 50% (EwW-R) exhibited structural defects. On E8, there was no difference in body growth among four groups of quail embryos that showed vital signs. On E15-16, the BW and BL were significantly ( $P < 0.01$ ) lower in EwW and EwW-R than in CT. There was no difference, however, in the degree of BW and BL reduction between EwW and EwW-R groups. Also, delayed development of glomeruli and a tendency toward adrenal gland enlargement were seen in these groups. In E8 CT kidneys,  $\alpha$ -SMA was expressed in renal arteries and arterioles, glomerular mesangium, and interstitial pericytes.  $\alpha$ -SMA signals in the glomerular mesangium were less distinguished in EwW groups.

### [Summary and Conclusion]

These results suggest that partial withdrawal of egg white before incubation induces

structural defects and early death, possibly due to the mechanical stress of egg white withdrawal. The fact that immediate return of withdrawn egg white did not restore decreased body growth at later embryonic days suggests that retarded growth is likely due to the consequence of stressful events rather than reduced nutrition (protein). The tendency toward adrenal gland enlargement in EwW and EwW-R groups supports this notion.