

Comparison of historical control data for maternal and fetal parameters in Sprague-Dawley and Wistar rats in prenatal developmental toxicity studies

出生前発生毒性試験におけるSprague-Dawley系ラットおよびWistar系ラットの母体・胎児指標の背景データ比較

- Naoki Aizawa, Takafumi Ohta, Haruka Moriyama, Jun Tsuchida, Yuka Sasaki, Hitoshi Katou, Tsuyoshi Higuchi
- Research Unit II, Drug Discovery Innovation Center, Mediford Corporation



Objective

In prenatal developmental toxicity studies (OECD TG 414), Sprague-Dawley (SD) rats are widely used, whereas Wistar rats are also used in some studies. Although understanding strain differences is important, few studies have compared these two strains at the same facility under the same conditions, and the appropriateness of test system selection has not been sufficiently evaluated. Therefore, this study compared inter-strain differences using data from SD and Wistar rats obtained at our institute.

Materials and Methods

- **Historical Control Data (HCD)**
 - Crl:CD(SD), 8 studies
 - Iar:Wistar-Imamichi, 7 studies
- **Examination items**
 - Dams: body weight, food consumption, cesarean section, gravid uterine weight, uterus weight, corrected body weight
 - Fetuses: anogenital distance, sex ratio, external examination, placental examination, fetal body weight, visceral examination, skeletal examination (Includes degree of ossification)

Results and Conclusion

Results:

Strain differences were observed in fetal visceral and skeletal examination. In the visceral examination, the incidences of thymic remnant in the neck and dilated renal pelvis were lower in Iar:Wistar-Imamichi rats than in Crl:CD(SD) rats. In the skeletal examination, the incidences of bipartite ossification of thoracic vertebral centra, cervical ribs, complete supernumerary ribs, and short supernumerary ribs were lower in Iar:Wistar-Imamichi rats, whereas the incidences of abnormal sternebraal alignment and bipartite ossification of sternebrae were higher. No clear strain differences were observed in maternal body weight, food consumption, cesarean section parameters, gravid uterine weight, corrected body weight, fetal anogenital distance external examination findings, placental observations or fetal body weight.

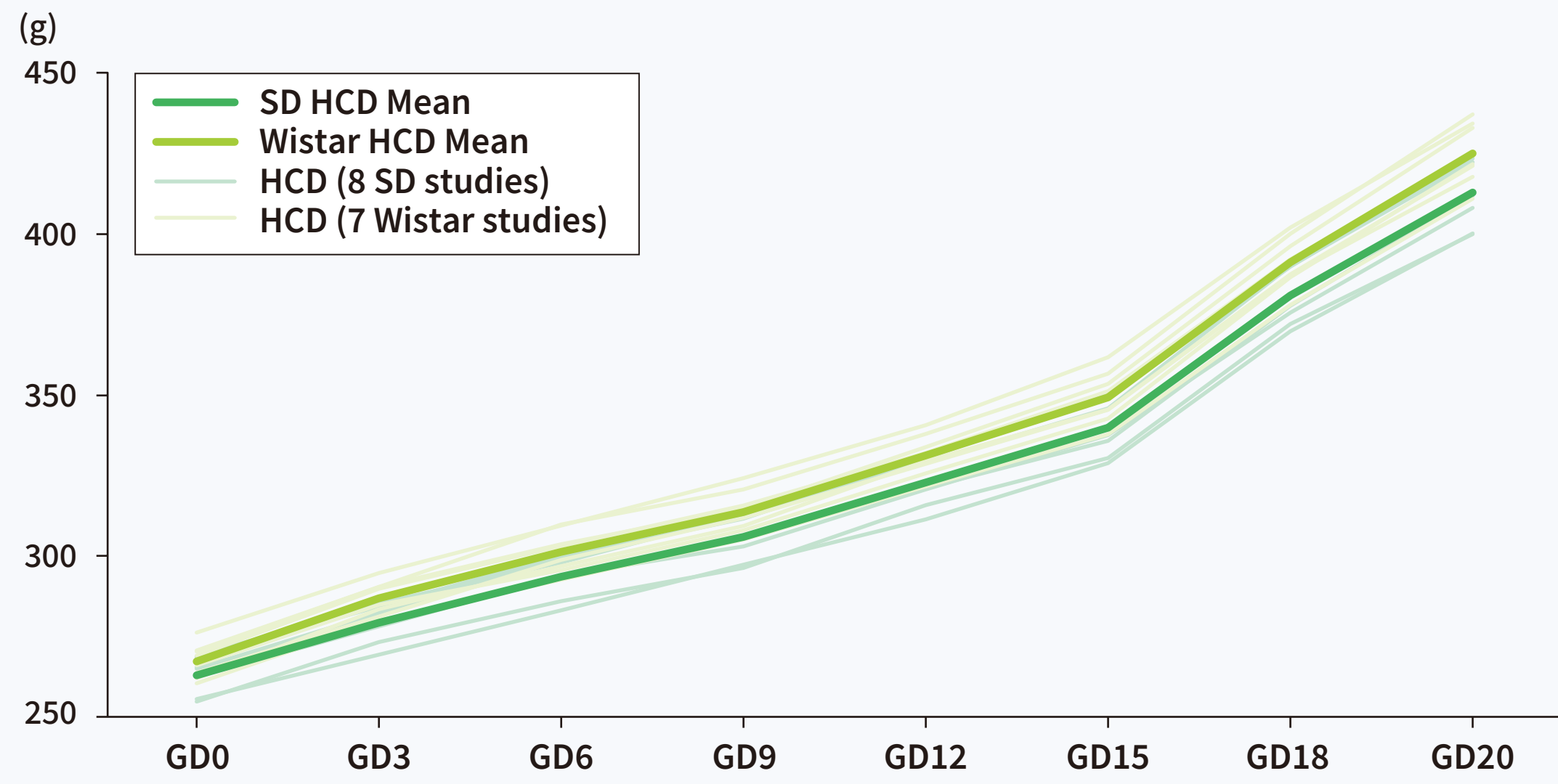
Conclusion:

No clear strain differences were observed in maternal parameters, whereas strain-specific differences were observed in fetal visceral and skeletal findings.

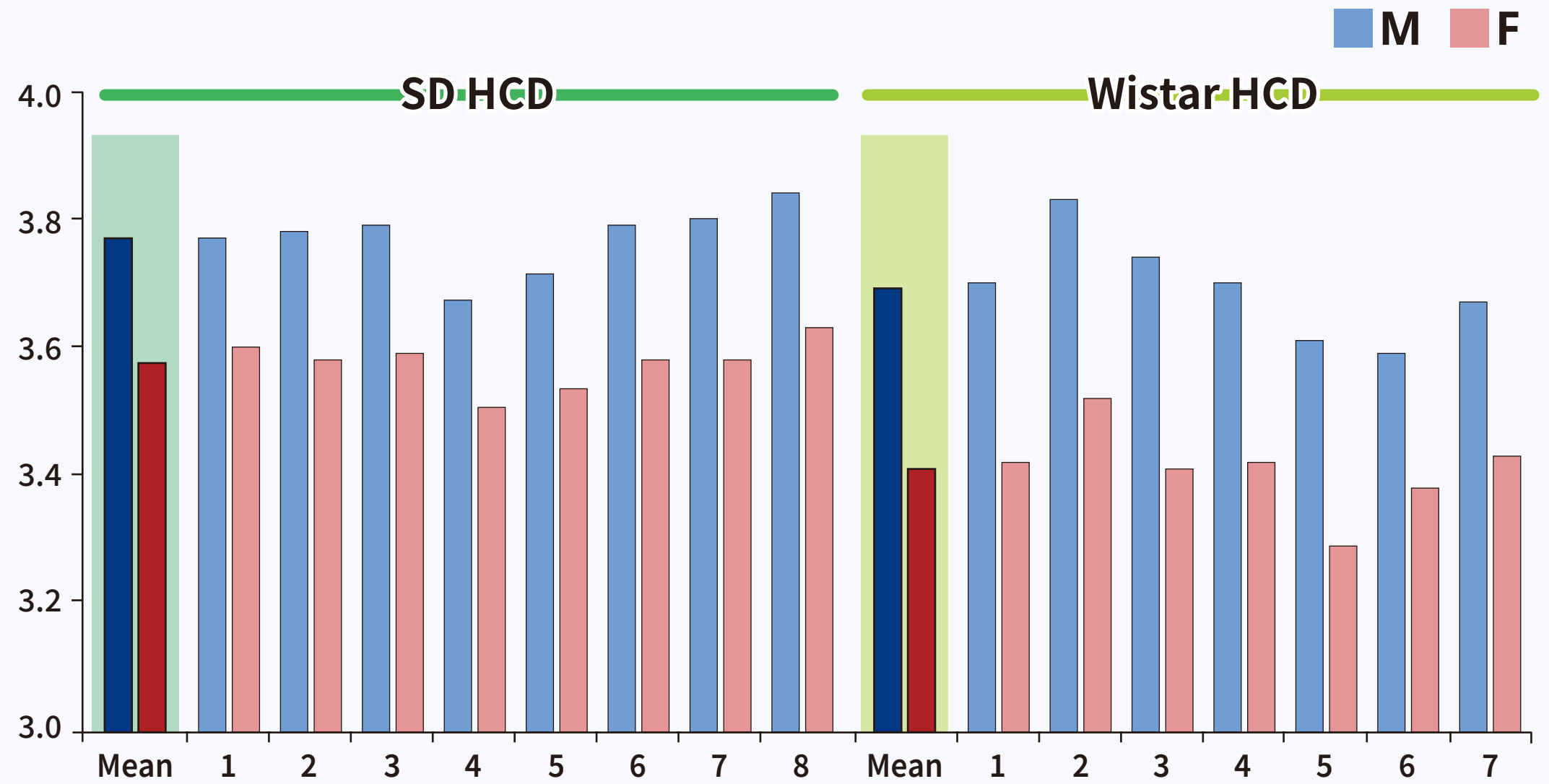
These results suggested that strain characteristics should be considered when interpreting historical control data HCD and selecting test systems.

Results

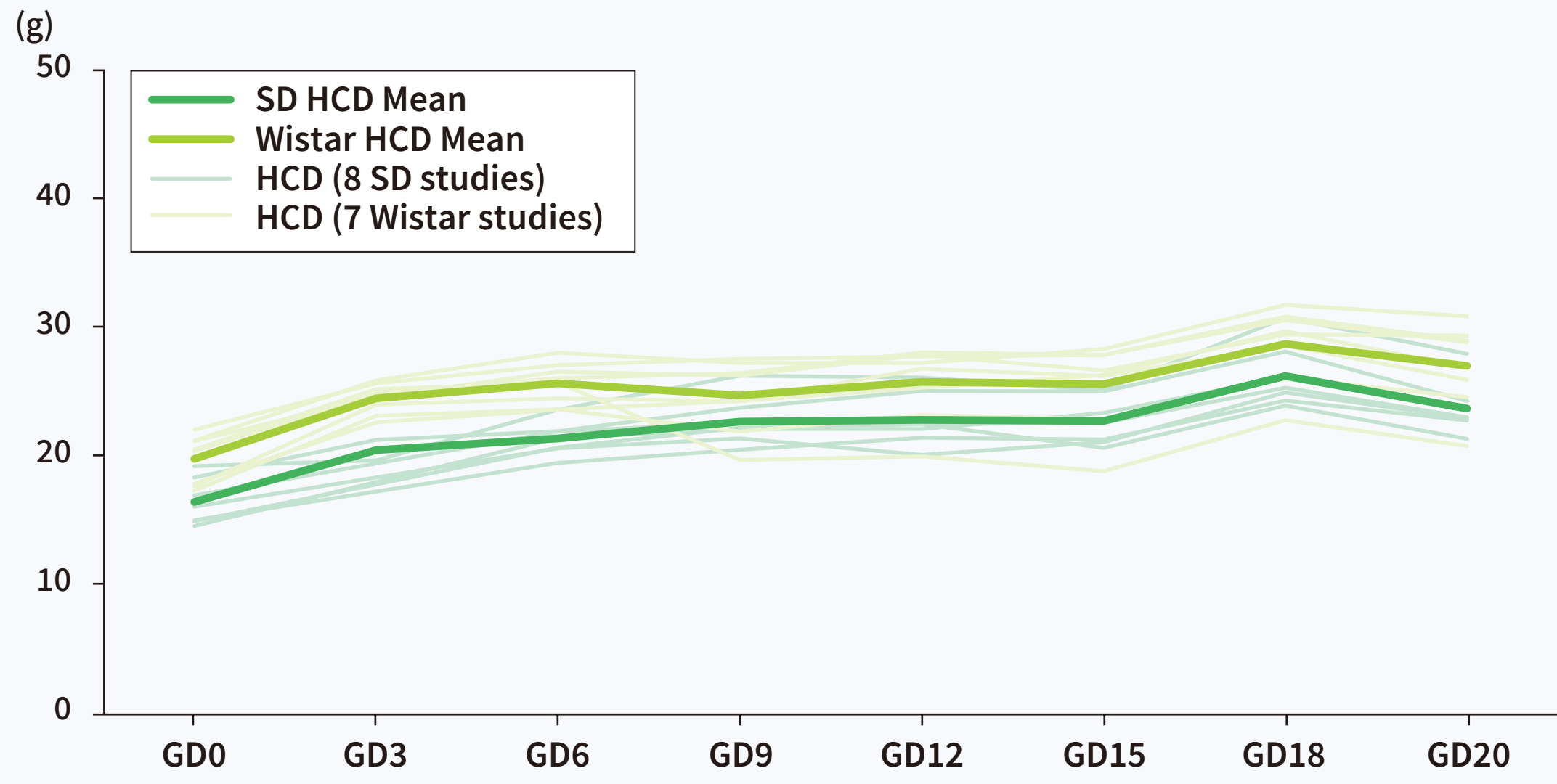
Body Weight



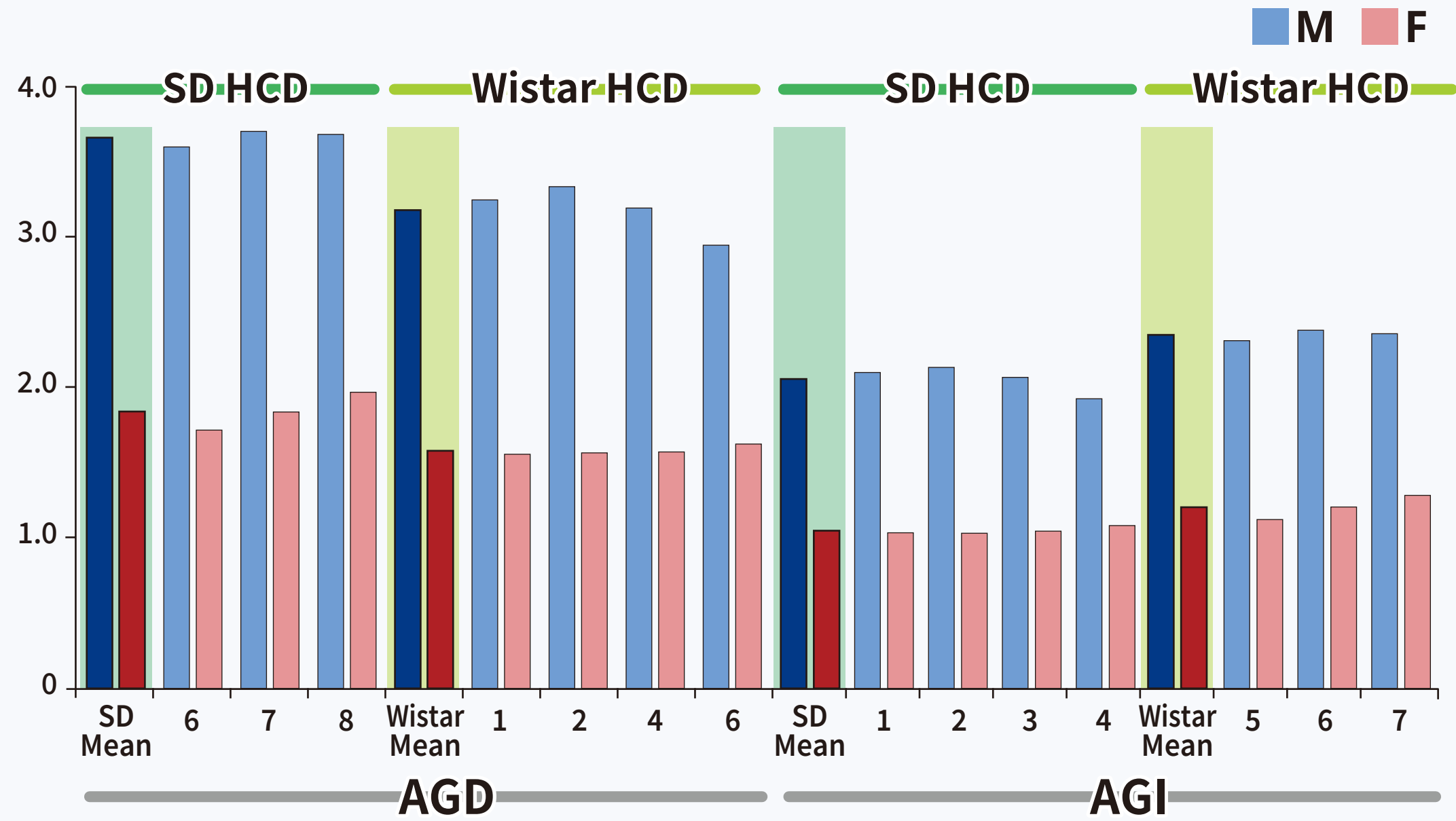
Body Weight of Fetuses (GD 20)



Food Consumption



Anogenital Distance



Cesarean Section Examination

	Crl:CD (SD)								Iar: Wistar-Imamichi							
	1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8
Observation on Cesarean Section	19	20	19	20	20	20	20	20	10	8	8	23	8	23	8	8
No. of dams	19	20	19	20	20	20	20	20	10	8	8	23	8	23	8	8
No. of corpora lutea	293	307	276	323	316	303	311	323	174	147	147	403	134	419	140	140
No. of implantations	278	295	256	311	299	284	299	306	152	135	140	384	131	398	134	134
No. of pre-implantation loss	15	12	12	12	13	17	12	12	17	15	15	25	12	33	5	5
No. of dead implants	21	16	13	14	17	15	12	12	13	13	13	19	19	21	6	6
Early resorptions	21	16	13	14	17	15	12	12	13	13	13	19	19	21	6	6
Late resorptions	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dead fetuses	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
No. of live fetuses	257	279	243	297	286	269	287	294	147	120	121	399	119	365	126	126
Sex ratio M/(M+F)(%)	0.95	1.16	0.96	1.03	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9	0.9
Weight of fetuses (g)	3.77±0.41	3.78±0.25	3.79±0.24	3.673±0.322	3.714±0.269	3.79±0.26	3.80±0.30	3.84±0.35	3.70±0.20	3.83±0.23	3.74±0.23	3.70±0.23	3.61±0.21	3.59±0.18	3.67±0.18	3.67±0.18
Male	3.60±0.29	3.58±0.20	3.59±0.28	3.506±0.339	3.535±0.209	3.58±0.23	3.58±0.27	3.63±0.37	3.42±0.20	3.52±0.17	3.41±0.25	3.42±0.24	3.29±0.27	3.38±0.17	3.43±0.19	3.43±0.19

Fetal Visceral Examination (Malformation)

	Crl:CD (SD)								Iar: Wistar-Imamichi							
	1	2	3	4	5	6	7	8	1	2	4	6	6	6	6	6
Visceral (Anomalies)	19	20	19	20	20	20	20	20	10	8	23	23	23	23	23	23
No. of animals (FO)	134	145	128	153	148	143	155	157	78	65	189	192	192	192	192	192
No. of fetuses examined	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Frequencies	(0.75)															
Dilated lateral ventricle	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Retrosophageal subclavian	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Absent kidney	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Absent uterine horn	0	(0.75)														

Fetal Skeletal Examination (Malformation)

	Crl:CD (SD)								Iar: Wistar-Imamichi							
	1	2	3	4	5	6	7	8	1	2	4	6	6	6	6	6
Skeletal (Anomalies)	19	20	19	20	20	20	20	20	10	8	23	23	23	23	23	23
No. of animals (FO)	134	145	128	153	148	143	155	157	78	65	189	192	192	192	192	192
No. of fetuses examined	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Frequencies	(0.75)															
Absent cervical vertebra	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Split cervical arch	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Fused cervical arch	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Absent thoracic vertebra	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Thoracic hemivertebra	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Hemicentric thoracic centrum	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Absent rib	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Short rib	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Fused sternebra	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Fetal Skeletal Examination (Degree of Ossification)

	Crl:CD (SD)								Iar: Wistar-Imamichi							
	1	2	3	4	5	6	7	8	1	2	4	6	6	6	6	6
Skeletal (Degree of ossification)	19	20	19	20	20	20	20	20	10	8	23	23	23	23	23	23
No. of animals (FO)	134	145	128	153	148	143	155	157	78	65	189	192	192	192	192	192
No. of fetuses examined	8.14±0.69	7.88±0.48	8.22±0.34	7.613±0.488	7.7±0.04	8.0±0.4	8.0±0.3	7.9±0.4	8.1±0.4	7.5±0.5	7.4±0.5	7.4±0.5	7.4±0.5	7.4±0.5	7.4±0.5	7.4±0.5
No. of sacrocaudal body	5.69±0.28	5.77±0.22	5.80±0.20	5.612±0.467	5.838±0.222	5.5±0.4	5.7±0.3	5.9±0.2	5.9±0.1	6.0±0.1	5.8±0.3	5.8±0.2	5.8±0.2	5.8±0.2	5.8±0.2	5.8±0.2
No. of sternebrae																

Fetal Visceral Examination (Variation)

	Crl:CD (SD)								Iar: Wistar-Imamichi							
	1	2	3	4	5	6	7	8	1	2	4	6	6	6	6	6
Visceral (Anomalies)	19	20	19	20	20	20	20	20	10	8	23	23	23	23	23	23
No. of animals (FO)	134	145	128	153	148	143	155	157	78	65	189	192	192	192	192	192
No. of fetuses examined	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Frequencies	(4.88)	(8.96)	(4.35)	(6.90)	(2.89)	(5.5)	(6.5)	(6.5)	(1.8)	(0.5)	(1.1)	(1.1)	(1.1)	(1.1)	(1.1)	(1.1)
Thymic remnant in the neck	2	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dilated renal pelvis	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Dilated ureter	3	8	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Fetal Skeletal Examination (Variation)

	Crl:CD (SD)								Iar: Wistar-Imamichi							
	1	2	3	4	5	6	7	8	1	2	4	6	6	6	6	6
Visceral (Anomalies)	19	20	19	20	20	20	20	20	10	8	23	23	23	23	23	23
No. of animals (FO)	134	145	128	153	148	143	155	157	78	65	189	192	192	192	192	192
No. of fetuses examined	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Frequencies	(25.37)	(18.62)	(17.5)	(18.75)	(15.58)	(15.1)	(19.2)	(8.6)	(12.9)	(17.5)	(16.3)	(16.3)	(16.3)	(16.3)	(16.3)	(16.3)
Bipartite ossification of supraoccipital	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Unossified thoracic centrum	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Bipartite ossification of thoracic centrum	2	3	4	4	2	2	2	3	0	0	0	0	0	0	0	0
Cervical rib	1	2	0	2	1	0	3	0	0	0	0	0	0	0	0	0
Full supernumerary rib	5	7	0	7	3	3	3	3	0	0	0	0	0	0	0	0
Short supernumerary rib	3	7	0	7	3	3	3	3	0	0	0	0	0	0	0	0
Wavy rib	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Misaligned sternebra	2	4	0	4	2	2	2	2	0	0	0	0	0	0	0	0
Bipartite ossification of sternebra	1	1	0	1	1	1	1	1	0	0	0	0	0	0	0	0
Bipartite ossification of lumbar centrum	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7 lumbar vertebrae	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5 lumbar vertebrae	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0