Table II. *Age-specific values in hematology in microminipig.*

			Age (months)					
Parameters	Unit	Gender	0-2 (M=9, F=10)	3-5 (M=6, F=8)	6-8 (M=6, F=8)	9-12 (M=9, F=17)	13-24 (M=14, F=13)	25-34 (M=14, F=10)
Reticulocytes	%	M+F	6.59±6.97	0.87±0.72	0.67±0.34	0.56±0.34	0.84±0.71	0.90±0.82
		M	7.98±7.56	0.45±0.16	0.66±0.35	0.53±0.22	0.94±0.88	1.08±0.65
		F	5.35±6.55	1.19±0.82*	0.67±0.35	0.59±0.44	0.70±0.35	0.76±0.94
Eosinophils	%	M+F	1.25±0.99	2.71±1.53	2.76±1.79	2.23±0.94	3.03±1.40	2.84±1.43
		M	1.26±1.23	2.42±1.59	2.58±2.12	2.51±1.02	2.94±1.10	3.58±1.30
		F	1.25±0.78	2.94±1.56	2.86±1.65	1.92±0.78	3.16±1.78	2.29±1.34
Basophils	%	M+F	1.19±0.32	0.91±0.19	0.95±0.35	0.84±0.26	0.95±0.32	1.04±0.30
		M	1.21±0.29	0.95±0.24	0.93±0.49	0.77±0.26	0.79±0.21	0.95±0.19
		F	1.17±0.36	0.89±0.15	0.96±0.27	0.92±0.24	1.16±0.33**	1.10±0.36
Monocytes	%	M+F	3.6±1.0	4.3±0.4	5.1±1.5	5.7±1.2	5.4±1.2	5.6±1.3
		M	4.5±2.0	4.5±0.9	5.1±1.1	6.0±1.0	5.4±1.3	6.6±0.8
		F	5.3±2.3*	4.7±1.2	5.1±1.7	5.4±1.3	5.5±1.0	5.0±1.1*
Lymphocytes	%	M+F	71.5±8.7	61.8±10.6	58.6±9.9	55.7±12.1	56.1±12.3	53.6±10.1
		M	67.3±11.0	63.9±8.0	54.8±10.9	53.2±13.0	51.3±12.6	51.8±8.7
		F	63.5±11.8	65.5±5.6	60.6±9.1	58.4±10.8	62.9±8.2	55.0±11.5
Neutrophils	%	M+F	24.5±9.4	26.4±8.5	31.1±10.7	33.8±11.7	32.7±11.9	35.1±10.4
		M	21.2±7.2	29.3±11.3	35.0±11.8	35.9±12.9	38.0±11.6	35.8±8.7
		F	27.5±10.4	24.3±5.5	29.0±9.8	31.6±10.2	25.2±8.1**	34.7±12.1
Large unstained cells	%	M+F	1.23±0.78	1.48±0.58	1.53±0.61	1.69±0.85	1.87±1.02	1.76±0.93
		M	1.26±0.64	1.20±0.47	1.58±0.45	1.64±0.60	1.67±0.97	1.40±0.53
		F	1.21±0.92	1.69±0.59	1.50±0.70	1.75±1.07	2.14±1.09	2.04±1.10
Eosinophils	$10^3/mm^3$	M+F	0.26±0.31	0.43±0.30	0.31±0.18	0.25±0.11	0.31±0.16	0.29±0.14
		M	0.29±0.43	0.33±0.22	0.29±0.20	0.27±0.11	0.29±0.12	0.35±0.11
		F	0.22±0.18	0.51±0.35	0.32±0.18	0.23±0.10	0.34±0.21	0.24±0.14
Basophils	$10^3/mm^3$	M+F	0.22±0.10	0.14±0.06	0.11±0.04	0.09±0.03	0.10±0.04	0.11±0.03
		M	0.24±0.12	0.13±0.05	0.10±0.04	0.08±0.02	0.08±0.02	0.09±0.02
		F	0.19±0.07	0.14±0.06	0.11±0.04	0.11±0.03*	0.12±0.04**	0.12±0.03
Monocytes	$10^3/mm^3$	M+F	0.85±0.57	0.67±0.25	0.60±0.23	0.65±0.21	0.55±0.13	0.58±0.15
		M	0.75±0.48	0.57±0.15	0.62±0.28	0.67±0.21	0.54±0.14	0.63±0.09
		F	0.95±0.64	0.75±0.29	0.59±0.22	0.63±0.21	0.57±0.13	0.54±0.18
Lymphocytes	$10^3/mm^3$	M+F	11.7±4.0	9.4±3.0	6.8±1.4	6.2±1.3	5.7±1.5	5.5±1.3
		M	13.3±4.8	8.1±1.8	6.4±1.4	5.7±1.1	5.1±1.5	5.0±1.0
		F	10.2±2.7	10.4±3.5	6.9±1.5	6.7±1.4*	6.5±1.0*	5.9±1.4
Neutrophils	$10^3/mm^3$	M+F	4.6±2.9	3.9±1.6	3.9±2.7	4.1±2.3	3.4±1.4	3.8±2.0
		M	4.3±3.1	3.9±1.9	4.8±4.1	4.3±2.5	3.8±1.5	3.6±1.3
		F	4.8±2.8	3.9±1.5	3.4±1.4	3.8±2.1	2.7±1.2	4.0±2.5
Large unstained cells	$10^3/mm^3$	M+F	0.21±0.15	0.23±0.14	0.18±0.08	0.20±0.11	0.20±0.13	0.19±0.13
		M	0.24±0.19	0.16±0.07	0.20±0.09	0.19±0.10	0.17±0.11	0.13±0.04
		F	0.18±0.12	0.28±0.16	0.17±0.08	0.20±0.13	0.23±0.14	0.23±0.15

M: males, F: females. *p<0.05, **p<0.01, significantly differerent from male.

However, the ratio of APTT to PT was different from that in other experimental animals. Although PT and APTT are commonly used as plasma-based assays for the assessment of coagulation activity in experimental animals, the exact time of each assay differs between species (12). In all species, except the rat (F344 strain), APTT is reported to be longer than PT and the ratio of APTT to PT is between 2:1 and 3:1. By contrast, in the MMPig, APTT is shorter than PT and the ratio is 0.88:1. Short APTT (11.2±1.0 s) as observed in the MMPig is a unique characteristic when compared with previously reported results for minipigs; the APTT in the Gottingen minipig is in the range of 26 to 46 s and that for the Yucatan minipig an average of 15.46±1.15 s. APTT is longer than PT in both minipig species, consistent with other species (13, 14). Although it will be necessary to elucidate the biological mechanism of the shorter APTT observed in the MMPig, this hypercoagulable response to the intrinsic pathway may suggest a thrombotic tendency in the MMPig.

APTT is assayed to evaluate the coagulation pathway, but does not fully reflect the interaction of coagulation factors or platelets *in vivo*. The newly developed microchip-based flow chamber system (WTF assay) mimics *in vivo* blood flow and is influenced by both platelet activation and coagulation reactions over the collagen/tissue thromboplastin-coated surface (10). In this experiment, we used flow rates of 10 μl/min, corresponding to initial wall shear rates of 600 s^{-1}, which simulates arterial blood flow in small to medium-sized arteries (15). T80 in the MMPig was 404.5±57.4 min compared with 558±90 in Man, and the WTF assay indicated that white thrombus formation in the microminipig was markedly more rapid than that in human (10). This result further supports the conjecture that the MMPig has a thrombotic tendency, at least by *in vitro* thrombus formation assay.

Conclusion

In this study, we demonstrated age-dependent changes in hematological and coagulation parameters for MMPigs. All hematological parameters were within the normal range, with no major sex or age difference. APTT in the MMPig was shorter than PT and the ratio of APTT to PT was 0.88:1. We also investigated thrombus formation activity and indicated a thrombotic tendency in the MMPig. These results could be useful to life science researchers in regard to the use of the MMPig as an experimental model animal for thrombus formation.

Conflicts of Interest

TN and HS are employees of Fujimori Kogyo Co., Ltd. TI and IM hold endowed faculty positions in thrombosis research and have received funds from Medipolis Medical Research Institute, Shin Nippon Biomedical Laboratories, Asahi Kasei Pharma, and Asahi Kasei Medical.

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