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Decrease in Polyamines with Aging and Their Ingestion from Food and Drink

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Changes in polyamine levels during aging were measured in 3-, 10- and 26-week-old female mice. The level of polyamines in pancreas, brain, and uterus was maintained during these periods. The level of spermidine slightly decreased in intestine, and decreased significantly in thymus, spleen, ovary, liver, stomach, lung, kidney, heart and muscle during these periods. In skin, the level of spermidine was maximal in 10-week-old mice and markedly reduced in 26-week-old mice. The results suggest that maintenance of polyamine levels may play important roles in the function of the pancreas, brain and uterus in 3- to 26-week-old mice. We next looked for polyamine-rich food materials as a dietary source of polyamines. Foods found to be rich in polyamines included wheat germ, rice bran, black rice, Philippine mango, green pepper, Japanese pumpkin, nuts, fermented pickles, pond smelt, turban shell viscera, whelk viscera, salted salmon roe, salted cod roe, beef intestine (boiled) and liver of eel, beef, pork and chicken; and, as previously reported, soybean, fermented soybean (*natto*), mushrooms, orange and green tea leaf. These results offer useful information when it becomes necessary to ingest polyamines from food.

Key words: aging, food, health, polyamines, tissue.

Polyamines (putrescine, spermidine and spermine) are present at millimolar concentrations in both prokaryotic and eukaryotic cells and play regulatory roles in cell growth (*1–3*). Stimulation of cell growth by polyamines is mainly due to the enhancement of specific kinds of protein syntheses which are important for cell growth (*4–7*). Accordingly, it is important to keep the polyamine content at an optimal level to maintain the function of various organs. However, it is known that polyamine content decreases with the progress of cell growth in *Escherichia coli* (*8*) and that polyamine content in six different rat tissues decreases with aging (*9*). The intracellular levels of polyamines are regulated at various steps including synthesis, degradation, uptake and excretion (*10*, *11*). The importance of polyamine ingestion from food was suggested by the finding that the antitumor effects of the inhibitors of polyamine biosynthesis were enhanced in mice bearing P388 leukemia or Lewis lung carcinoma when a polyamine-deficient diet was used (*12*). It has been also shown that polyamines are readily taken up by the gut and enter the systemic circulation in rats (*13*, *14*) and mice (*12*). To keep the polyamine content at an optimal level in various organs, it is presumably important to ingest polyamines from food as people become older, because it is known that the activity of one of the key polyamine biosynthetic enzymes, ornithine decarboxylase, decreases with increasing age in rats (*15*). In this context, the polyamine contents in 70 typical kinds of food were measured previously (*13*, *16*).

In this communication, polyamine contents in 227 kinds of food and drink were measured. Furthermore, polyamine levels in 14 different tissues were measured using 3-, 10- and 26-week-old female mice to confirm that polyamine contents in some tissues decreased with increasing age.

MATERIALS AND METHODS

Materials—Female C57BL/6 mice aged 3 to 26 weeks were purchased from Japan SLC Inc. Three-week-old mice used were those right after separation from dams. The mice were maintained on laboratory chow and tap water *ad libitum*, and killed around 1 PM. Muscle was obtained from leg, and intestine used was a 3-cm length of the middle part. Brain contained whole cerebrum and cerebellum. Food materials and beverages were obtained from local and special markets. Human milk was obtained during the first postnatal month with informed consent of the donors.

Measurement of Polyamines—Polyamine levels in various mice tissues and foods were determined by use of a Toyo Soda HPLC system as described previously (*17*) with a slight modification. Foods were frozen in liquid nitrogen, cut into small pieces and homogenized with 5% trichloroacetic acid (TCA). Mouse tissues were cut into small pieces and homogenized with 5% TCA. The homogenates were centrifuged at 4,000 × *g* for 10 min at 4°C, and polyamine levels in the supernatant were analyzed. Values were shown as nmol/mg protein. Since the content of amino acids was high in food, two tandem TSK gel polyaminepak columns (4.6 × 50 mm) were used to separate polyamines from amino acids. The components of the elution buffer and the *o*-phthalaldehyde solution are described in the

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previous communication (*17*). The flow rate of the elution buffer and the *o*-phthalaldehyde solution were 0.2 ml/min, and fluorescence was measured at an excitation wavelength of 340 nm and an emission wavelength of 455 nm. The retention times for putrescine, cadaverine, spermidine, agmatine and spermine were 27, 38, 51, 89 and 102 min, respectively. Values shown in the table (nmol/g wet weight) are means of duplicate determinations of each sample. Polyamine contents in each food were measured using at least two different samples. If the difference in polyamine contents of the two samples was large, both values are shown in the Table 1.

Measurement of Protein Content—Protein content in mouse tissues was measured using 5% TCA precipitate according to the method of Lowry *et al*. (*18*).

RESULTS

Polyamine Content in Tissues of 3- to 26-Week Old Mice—Polyamine levels in 14 different tissues were measured using 3-, 10- and 26-week-old mice (Fig. 1). Except in kidney and heart, spermidine content was the highest among the three polyamines. In kidney and heart, spermine content was the highest. The level of spermidine in tissues of 3-week-old mice was in the order pancreas > thymus > spleen > ovary = uterus = intestine = liver > stomach > lung > kidney = brain > skin > heart > muscle. The concentration of spermidine in pancreas of 3-week-old mice was estimated as approximately 5 mM, assuming that 1 mg of cellular protein corresponds to 5 μl of cell volume (*19*).

The level of polyamines in pancreas, brain and uterus was maintained in 3- to 26-week-old mice. The level of spermidine slightly decreased in intestine, and it significantly decreased in thymus, spleen, ovary, liver, stomach, lung, kidney, heart and muscle during these periods. A decrease in spermidine of more than 50% in 10-week-old compared to 3-week-old mice was observed in liver, kidney, heart and muscle. In skin, the level of spermidine was maximal in 10-week-old mice, and there was a pronounced decrease between 10 and 26 weeks. The change of putrescine and spermine in these tissues was not significant in 3- to 26-week-old mice, except for the decrease in spermine in skin, heart and muscle. The results confirmed previous results (*9*) that polyamine content in various tissues decreased with aging except in pancreas, brain and uterus.

Polyamine Analysis of Food Materials—Polyamine contents of 227 kinds of food and drink were measured. Among grains, polyamine levels were high in rice bran, wheat germ and black rice. Thus, rice mixed with black and brown rice, and bread mixed with wheat germ are recommended as a source of polyamines. Among vegetables, beans, seeds and mushrooms, the following were rich in polyamines: green pepper, broccoli, broccoli sprout, Japanese radish leaf, turnip leaf, Japanese pumpkin, all kinds of beans, fermented soybeans (*natto*), pine seed, nuts and all kinds of mushrooms. Putrescine and cadaverine were included in fermented cheese and pickles, especially in blue cheese, shibazuke (*Lactobacillus*-fermented cucumber) and nukazuke (*Lactobacillus*-fermented cucumber with salted rice-bran paste). It has been reported that spermine in human milk prevents the occurrence of allergies in children (*20*). Our data confirmed the presence of spermine in human milk, but not in bovine milk. Among fish, shellfish and meat, polyamines were rich in pond smelt, turban shell viscera, whelk viscera, salted cod roe, salted salmon roe, codfish milt, beef intestine (boiled), and liver of eel, beef, pork and chicken. Among fruits, putrescine levels were high in orange and Philippine mango, and spermidine levels were high in durian and Philippine mango. Putrescine and cadaverine were also present in soy sauce, soybean paste and fish sauce. Among beverage and alcohol, polyamines were included in green tea leaf. However, polyamines contents were low in green tea extracted from green tea leaf. Agmatine was rich in Japanese sake (rice wine). Putrescine was included more in beer than in wine. Sake lees contained putrescine, cadaverine and agmatine.

It has been reported that the optimal concentrations of spermine, spermidine and putrescine for stimulation of globin synthesis are 0.08, 0.4 and 8 mM, respectively (*21*). The effect of cadaverine was nearly equal to that of putrescine (*22*), and that of agmatine was less than that of putrescine (*23*). Since the effective concentration of each polyamine on cell growth was nearly parallel with that of protein synthesis (*21*), it is thought that polyamines are effective in the order spermine > spermidine > putrescine = cadaverine > agmatine in terms of stimulating cell growth. The content of spermine in food was in the order turban shell viscera (770–32,700 nmol/g) > chicken liver > pork liver > beef liver > wheat germ > salted cod roe > beef intestine (boiled) > chicken heart > eel liver > Japanese pumpkin. Spermine content in these foods was more than 500 nmol/g. The content of spermidine was in the order turban shell viscera (166–91,500 nmol/g) > wheat germ > agaricus dried > black soybean > soybean > shimeji mushroom > eringi mushroom > fermented soybean (*natto*) > green pepper > maitake mushroom. Spermidine content in these foods was more than 700 nmol/g. The content of putrescine was in the order green pepper (1,180–2,690 nmol/g) > pond smelt > shibazuke (*Lactobacillus*-fermented cucumber) > orange > codfish milt > nukazuke (*Lactobacillus*-fermented cucumber with salted rice-bran paste) > matsutake mushroom > Philippine mango > oyster sauce > corn. Putrescine content in these foods was more than 800 nmol/g. The content of cadaverine was in the order fish sauce (*nam pla*) (3,900 nmol/g) > gorgonzola cheese > pond smelt > fermented soybeans (*natto*) > blue cheese > whelk viscera > sake lees > black soybean > soybean. Cadaverine content in these foods was more than 800 nmol/g. The content of agmatine was in the order sake lees (5,200 nmol/g) > Japanese sake > Japanese radish sprout > pond smelt (whole) (1,280 nmol/g).

We confirmed that foods rich in polyamines include soybean, fermented soybean (*natto*), mushrooms, orange and green tea leaf (*13*, *16*). We also found that other foods rich in polyamines include wheat germ, rice bran, black rice, corn, Philippine mango, green pepper, Japanese pumpkin, nuts, fermented pickles (shibazuke, nukazuke *etc.*), pond smelt, turban shell viscera, whelk viscera, beef intestine (boiled), and liver of eel, pork and chicken. The foods containing three kinds of polyamines were wheat germ, rice bran, green pepper, Japanese pumpkin, beans, turban shell viscera, whelk viscera, salted salmon roe, salted cod roe, beef intestine (boiled) and liver of eel.

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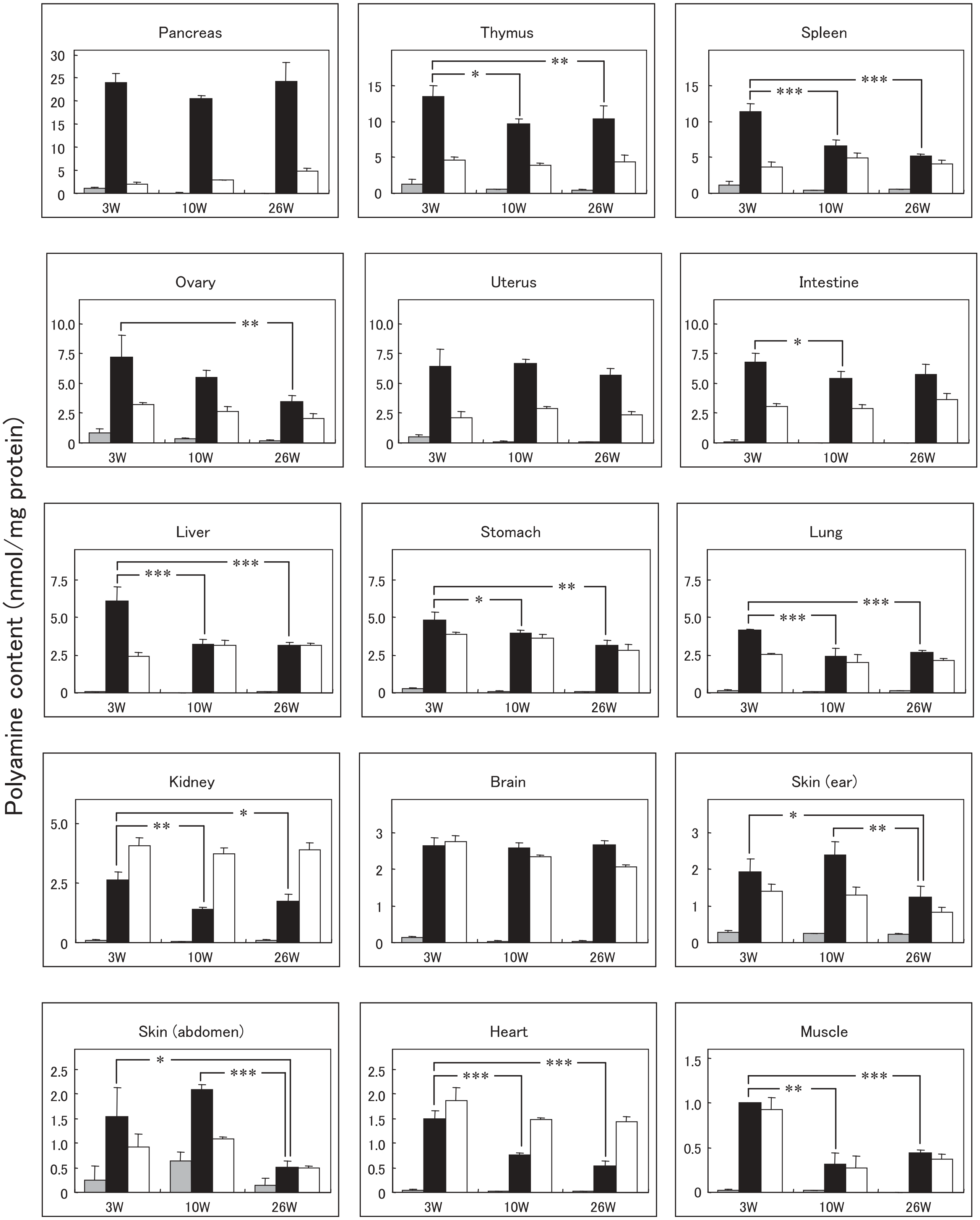

Fig. 1. **Level of polyamines in tissues of 3-, 10- and 26-week old mice.** The polyamine levels were measured as described in "MATERIALS AND METHODS." Values are mean ± SE of 5 mice. Gray column, putrescine; black column, spermidine; white column, spermine. Statistical significance of differences in spermidine level between 3-week-old mice and 10- or 26-week-old mice was evaluated using a two-tailed unpaired Student's t test. In skin, statistical significance of differences in spermidine level between 10-week-old and 26-week-old mice was also evaluated. $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

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Table 1. **Polyamine contents in food and drink.**

	Food or drink	Polyamine (nmol/g)				
		Putrescine	Spermidine	Spermine	Cadaverine	Agmatine
Grain						
1	rice	14	12	n.d.[a]	n.d.	n.d.
2	black rice (*Oryza sativa* subsp. *javanica*)	388	120	139	19	n.d.
3	brown rice (*Oryza sativa* L.)	56	44	49	20	n.d.
4	red rice (*Oryza sativa* subsp. *japonica*)	111	47	56	31	10
5	millet	19	63	48	9	n.d.
6	**rice bran**	**554**	**355**	**440**	**109**	**254**
7	barley	17	16	20	n.d.	n.d.
8	wheat flour	34	56	n.d.	198	n.d.
9	**wheat germ**	**706**	**2,440**	**721**	**300**	**190**
10	bread	15	21	21	23	n.d.
11	corn	198–842	298	6	447–20	n.d.
12	buckwheat flour	41	133	148	100	n.d.
13	grain amaranth (*Amarantus hypochondriacus* L.)	30	623	65	158	n.d.
Vegetable						
14	**green pepper**	**1,180–2,690**	**246–745**	**85–242**	**55**	**44–192**
15	orange paprika	59	52	18	2	n.d.
16	red paprika	24	27	17	3	n.d.
17	yellow paprika	54	34	23	<1	n.d.
18	broccoli	95–233	259–565	42	27–106	12
19	broccoli sprout	501	188	n.d.	98	307
20	garlic (grown in Japan)	3	86	28	62	n.d.
21	garlic (grown in China)	38	50–497	11	516	n.d.
22	eggplant	214	86	27	49	n.d.
23	Japanese radish sprout	496	128	n.d.	137	1,340
24	Japanese radish	17	54–144	n.d./16	16–69	n.d.
25	Japanese radish leaf	85	530	21	56–119	34
26	turnip	27	92	n.d.	17	n.d.
27	turnip leaf	219	405	19	42	n.d.
28	cabbage	161	117	n.d.	59	n.d.
29	lettuce	78	66	5	32	n.d.
30	watercress	20	201	7	158	32
31	mulukhiya	76–286	148–240	36	151–293	n.d.
32	rucola	14–122	101–200	31	194	n.d.
33	leek	70–767	66–205	32	172–436	n.d.
34	parsley	87	161	36	40	n.d.
35	bean sprout	4	174	159	258	26
36	tomato	272	24	4	16	n.d.
37	yellow tomato	85	36	4	28	n.d.
38	chicory	126	49	22	76	n.d.
39	field peas	29	173	120	124	n.d.
40	smartweed	70	220	17	109	n.d.
41	Japanese parsley	143	138	13	82	n.d.
42	edible chrysanthemum	65	118	22	58	n.d.
43	garland chrysanthemum	73	118	40	64	n.d.
44	green onion	279	117	<1	17	n.d.
45	onion	45	32	n.d.	287	n.d.
46	ginger	36	n.d.	n.d.	n.d.	n.d.
47	ginger root	10	27	7	53	n.d.
48	cucumber	112	71	n.d.	29	n.d.
49	cauliflower	42	284	22	81	n.d.
50	Chinese cabbage	69	108	n.d.	13	n.d.
51	perilla	35–437	73	46	46	n.d.
52	**Japanese pumpkin**	**263**	**188**	**529**	**17–113**	**n.d.**
53	okra	247	128	n.d.	70	n.d.
54	spinach	50	185	18	83	n.d.

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Table 1. *Continued*

	Food or drink	Polyamine (nmol/g)				
		Putrescine	Spermidine	Spermine	Cadaverine	Agmatine
55	bamboo shoot	747	n.d.	n.d.	436	n.d.
56	wasabi	85	93	13	n.d.	n.d.
57	rosemary	114	94	38	n.d.	n.d.
58	dill	144	201	43	238	n.d.
59	aloe	319	53	n.d.	n.d.	n.d.
60	echalote	31	58	7	84	n.d.
61	peppermint	78	91	10	30	n.d.
62	mitsuba (*Cryptotaenia japonica*)	16	63	18	n.d.	n.d.
63	ashitaba (*Angelica keiskei*)	49	230	30	180	4
64	sweet potato	15	20	29	8–261	n.d.
65	potato	96–255	86	17	217	n.d.
66	yam (*Dioscorea batatas*)	19	35	n.d.	24	n.d./8
67	taro (*Colocasia esculenta* Schott)	106	83	2	118	n.d.
68	lotus root	75–227	65	n.d.	72	25–141
69	carrot	65–160	55	n.d.	25	n.d.
70	burdock	54–134	48	34	296	n.d.
Beans and their products						
71	green soybeans	69–162	474	33–219	45–361	14
72	**soybean**	**400–650**	**1,090**	**290**	**804**	**59**
73	black soybean	198–648	557–1,210	187	206–816	n.d./131
74	azuki bean	33	679	367	264	n.d.
75	tofu	20	107	32	180	13
76	sheet of dried soybean casein	80	268	49	262	31
77	soybean milk	24	112	14	136	27
78	**fermented soybeans (*natto*)**	**129**	**600–1,060**	**88**	**1,990**	**387**
79	tempe	514	589	67	344	23
Seeds and nuts						
80	sesame	29	126	22	182	n.d.
81	watermelon seed	43	300	141	136	n.d.
82	pumpkin seed	121	248	114	132	488
83	pine seed	400	429	91	190	n.d.
84	**pistachio nut**	**488**	**256**	**105**	**32**	**5**
85	cashew nut	45	124	363	391	n.d.
86	sunflower seed	34	383	89	221	n.d.
87	almond	49	181	165	56	n.d.
88	ginkgo nut	12	n.d.	n.d.	48	n.d.
89	chestnut	59	278	63	13	n.d.
Mushrooms						
90	**shimeji (*Lyophyllum shimeji*)**	**122–514**	**396–1,090**	**n.d.**	**104**	**n.d.**
91	eringi (*Pleurotus eryngii*)	n.d.	1080	n.d.	211	590
92	maitake (*Grifola frondosa*)	134	728	n.d.	58	n.d.
93	shiitake (*Lentinus edodes*)	10	693	n.d.	76	n.d.
94	nameko (*Pholiota nameko*)	42–164	608	n.d.	30	n.d.
95	yamabushitake (*Hericium erinaceum*)	140	493	n.d.	129–560	n.d.
96	**dried agaricus (*Agaricus brazei murill*)**	**675**	**2,340**	**17**	**516**	**n.d.**
97	matsutake (*Tricholoma matsutake*)	1,030	399	n.d.	67	n.d.
98	enoki (*Flammulina velutipes*)	34	554	n.d.	158	n.d.
Milk and its products						
99	bovine milk	<1	<1	<1	<1	n.d.
100	human milk[b]	<1	3	6	1	n.d.
101	yogurt	n.d.	n.d.	n.d.	n.d./11	n.d.
102	processed cheese	n.d.	n.d.	n.d.	n.d.	n.d.
103	gorgonzola cheese	59	44	n.d.	3,760	n.d.
104	**blue cheese**	**189**	**262**	**n.d.**	**1110**	**7**
105	mozzarella cheese	n.d.	n.d.	n.d.	n.d.	n.d.

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Table 1. *Continued*

	Food or drink	Polyamine (nmol/g)				
		Putrescine	Spermidine	Spermine	Cadaverine	Agmatine
Pickles						
106	shibazuke (*Lactobacillus*-fermented cucumber)	1,450	63	9	334	n.d.
107	pickled cucumber	89	4	n.d.	18	n.d.
108	pickled Japanese apricot	5	12	n.d.	n.d.	n.d.
109	**nukazuke (*Lactobacillus*-fermented cucumber with salted rice-bran paste)**	**429–1,200**	**129**	**n.d.**	**565**	**n.d.**
110	koujizuke (*Aspergillus*-fermented cucumber)	112	63	n.d.	81	4
111	narazuke (yeast-fermented cucumber)	314	12	n.d.	15	318
112	lightly-pickled cucumber	70	105	n.d.	50	n.d.
Fish and shellfish						
113	conger	121	28	80	64	n.d.
114	angler	8	54	65	5	n.d.
115	angler liver	n.d.	225	200	n.d.	n.d.
116	sweet fish	106	65	45	15	n.d.
117	squid	n.d.	12	58	63	51
118	sardine	12	81	73	53	n.d.
119	alfonsino	10	11	22	12	n.d.
120	salmon	38	45	41	22	n.d.
121	saury	11	20	44	14	n.d.
122	shark	70	70	122	20	n.d.
123	sea bream	n.d.	15	24	12	n.d.
124	octopus	n.d.	n.d.	111	25	n.d.
125	scabbard fish	n.d.	17	20	10	n.d.
126	yellowtail	n.d.	18	56	n.d.	n.d.
127	tuna fish	10	20	77	18	n.d.
128	swordfish	13	14	89	21	n.d.
129	horse mackerel	5	21	28	73	n.d.
130	bonito	14	31	74	18	n.d.
131	dried small sardines	129	351	141	142	n.d.
132	codfish	22	62	51	30	n.d.
133	eel	109	110	57	42	32
134	**eel liver**	**420**	**548**	**546**	**43**	**n.d.**
135	shrimp	42	n.d.	n.d.	61	388
136	crab	11	n.d.	n.d.	44	14
137	**pond smelt (*Hypomesus nipponensis*)**	**1,490**	**156**	**160**	**2,520**	**1,280**
138	short-neck clam	6	18–121	307	30	n.d.
139	sea urchin	32	n.d.	166	404	n.d.
140	oyster	17	139	291	306	18
141	turban shell (*Turbo cornutus*)	2	36	402	24	18
142	**turban shell viscera**	**18–120**	**166–91,500**	**770–32,700**	**59**	**n.d.**
143	whelk (*Babylonia japonica*)	32	346	48	52	n.d.
144	**whelk viscera**	**43–743**	**104**	**483**	**158–977**	**n.d./124**
145	**corbicula (*Corbicula japonica*)**	**283–853**	**219–679**	**52**	**51**	**9**
146	**salted cod roe**	**906**	**241**	**603**	**77**	**n.d.**
147	**salted salmon roe**	**287**	**670**	**184**	**85**	**12**
148	codfish milt	780–1,270	65	415	26	n.d.
149	amberjack	n.d.	16	43	14	n.d.
150	mackerel	20	49	92	28	n.d.
151	young sardines	36	218	136	30	n.d.
152	white fish	119	160	75	27	n.d.
Meat						
153	beef	27	19	144	82	n.d.
154	pork	6	11	201	23	n.d./247
155	chicken	17	46	342	104	n.d.
156	duck	20	58	323	47	n.d.
157	lamb	11	34	233	44–150	n.d.

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Table 1. *Continued*

	Food or drink	Polyamine (nmol/g)				
		Putrescine	Spermidine	Spermine	Cadaverine	Agmatine
158	beef liver	12	47	974	193	n.d.
159	**beef intestine (boiled)**	**232**	**232**	**597**	**607**	**n.d.**
160	pork liver	27	232	1010	164	n.d.
161	**chicken liver**	**28**	**395**	**1380**	**202–575**	**n.d.**
162	chicken gizzard	12	104	427	38	n.d.
163	chicken heart	8–135	118	567	71	n.d.
164	goose liver paste	92	119	201	178	n.d.
165	chicken egg the white	n.d.	n.d.	n.d.	2	n.d.
166	chicken egg yolk	10	4	n.d.	261	n.d.
167	quail's egg the white	n.d.	n.d.	n.d.	16	n.d.
168	quail's egg yolk	8–62	5	n.d.	60–138	n.d.
Fruits						
169	white grapefruit	292	19	3	n.d.	n.d.
170	ruby grapefruit	580	20	n.d.	18	n.d.
171	**orange**	**620–1,360**	**27–93**	**n.d.**	**20**	**n.d.**
172	tangerine	860	80	n.d.	93	n.d.
173	lime	466	34	9	n.d.	n.d.
174	pear	17	20	n.d.	4	n.d.
175	strawberry	11	41	n.d.	42	n.d.
176	akebi (*Akebia quinata*)	33	n.d.	n.d.	n.d.	n.d.
177	persimmon	4	11	n.d.	37	n.d.
178	fig	25	36	n.d.	n.d.	n.d.
179	pomegranate (*Punica granatum punica*)	2	5	n.d.	27	n.d.
180	peach	4	42	25	<1	n.d.
181	blueberry	11	35	n.d.	6	n.d.
182	melon	5	81	n.d.	n.d.	n.d.
183	watermelon	n.d.	8	n.d.	8	n.d.
184	cherry	53	19	n.d.	n.d.	n.d.
185	prune	12	11	n.d.	20	n.d.
186	grape	106	87	n.d.	85	n.d.
187	apple	17	19	n.d.	n.d.	n.d.
188	banana	180–466	60	n.d.	106	73
189	durian	142	278	n.d.	33	n.d.
190	papaya	53	37	n.d.	n.d.	3
191	dragon fruit	13	23	n.d.	n.d.	n.d.
192	pineapple	46	30	n.d.	30	n.d.
193	kiwifruit	12	25	7	n.d.	n.d.
194	**Philippine mango**	**903**	**199**	**16**	**n.d.**	**n.d.**
195	avocado	n.d.	70	20	n.d.	n.d.
Seasoning						
196	soy sauce	304	89	n.d.	354	n.d.
197	soy sauce (*tamari*)	344	106	n.d.	390	n.d.
198	red soybean paste	221	n.d.	n.d.	39	20
199	white soybean paste	413	6	n.d.	612	17
200	black bean soy sauce	333	74	n.d.	700	n.d.
201	oyster sauce	873	114	33	358	60
202	**fish sauce (*nam pla*)**	**789**	**28**	**115**	**3,900**	**55**
203	rice vinegar	22	3	n.d.	2	n.d.
204	grain vinegar	77	4	<1	1	1
205	apple vinegar	<1	n.d.	n.d.	n.d.	n.d.
206	maple syrup	n.d.	n.d.	n.d.	n.d.	n.d.
207	honey	n.d.	n.d.	n.d.	n.d.	n.d.
Beverages						
208	**green tea leaf**	**173**	**296**	**177**	**281**	**n.d.**
209	black tea leaf	25	89	114	240	n.d.

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Table 1. *Continued*

	Food or drink	Polyamine (nmol/g)				
		Putrescine	Spermidine	Spermine	Cadaverine	Agmatine
210	coffee bean	n.d.	n.d.	n.d.	n.d.	n.d.
211	cocoa powder	n.d.	n.d.	n.d.	n.d.	n.d.
212	green tea	18	23	19	38	n.d.
213	black tea	6	8	11	26	n.d.
214	cola	n.d.	n.d.	n.d.	n.d.	n.d.
215	Japanese sake (1)	1	n.d.	n.d.	16	1,910
216	Japanese sake (2)	9	3	n.d.	5	666
217	sake lees (1)	119	2	n.d.	942	5,200
218	sake lees (2)	388	40	n.d.	631	295
219	dark beer	217	2	n.d.	17	40
220	beer (1)	297	3	n.d.	68	94
221	beer (2)	224	1	n.d.	29	88
222	white wine	40	n.d.	<1	5	n.d.
223	red wine	58	3	n.d.	2	n.d.
224	plum liqueur	46	2	<1	n.d.	n.d.
225	brandy	n.d.	n.d.	n.d.	n.d.	n.d.
226	vodka	n.d.	n.d.	n.d.	n.d.	n.d.
227	shochu (distilled spirit made from sweet potato)	n.d.	n.d.	n.d.	n.d.	n.d.

Polyamine contents in each food were measured using at least two different samples. When the polyamine contents in two samples differed appreciably, both values are shown in the table; otherwise, values are the mean of duplicate determinations. In the case of green tea and black tea, polyamines of 1 g tea leaf were extracted with 5 ml of hot water. Typical polyamine-rich food was shown in boldface. [a]n.d.; not detectable; [b]average of three persons.

DISCUSSION

In this study, the level of polyamines was measured using HPLC in 14 different tissues of 3-, 10- and 26-week-old mice and in 227 kinds of food and drink from the point of view of the maintenance of health in old age. It was reported about 40 years ago that spermidine and spermine contents in 6 different rat tissues (liver, thymus, spleen, kidney, muscle and brain) decreased with aging, as determined using an old technique of polyamine measurement by paper electrophoretic separation (*9*). The order of the decrease in spermidine content in these tissues was muscle > kidney > liver > spleen > thymus > brain, which was similar to our results. Although the levels of polyamines, especially spermidine, decreased in most tissues in mice, the levels in pancreas, brain and uterus were maintained between 3 and 26 weeks of age. Many digestive enzymes are synthesized in pancreas and many ion channels such as K^+ channels and NMDA receptors exist in brain. In uterus, protein synthesis may be active due to menstruation. Since stimulation of protein synthesis (*6*) and modulation of ion channels (*24*, *25*) are the most important functions of polyamines, mechanisms to maintain their levels may exist in these tissues. In human, polyamine content in maturating erythrocytes was reported to be lower than that in younger erythrocytes when they were age-separated by density (*26*).

In human, it has been reported that spermine deficiency is a cause of Snyder-Robinson syndrome (*27*); that spermine in human milk during the first postnatal month prevents the occurrence of allergies (*20*); and that administration of α-difluoromethylornithine (DFMO), an inhibitor of ornithine decarboxylase, causes hearing loss, although this may be due to a side effect of DFMO rather than the decrease in polyamine content (*28*, *29*). In mice or rats, a decrease in polyamines caused hair loss and infertility in females (*30*), pancreatitis (*31*), and impairment of spatial learning (*32*). Furthermore, ingestion of polyamines inhibited gastric ulceration (*33*) and stimulated maturation of intestine (*34*) in rats. On the contrary, the antitumor effects of polyamine biosynthesis inhibitors were enhanced in mice bearing P388 leukemia or Lewis lung carcinoma when a polyamine-deficient diet was used (*12*). These results suggest that ingestion of polyamine-rich food may be helpful for maintenance of health especially in old age. However, cancer patients should avoid polyamine-rich food, as mentioned above (*12*). Our results offer useful information about when it becomes necessary to ingest or to avoid ingestion of polyamines.

Since the decrease in spermidine was most marked among the three polyamines, either food containing the three polyamines or spermidine-rich food is recommended in the diet. In this respect, some food contained norspermidine [*N*-(3-aminopropyl)-1,3-diaminopropane], which is eluted at 45 min on HPLC under our experimental conditions and functions similarly to spermidine in the stimulation of protein synthesis (*22*). These foods are eggplant, tomato, gorgonzola cheese, shibazuke, pond smelt, soy sauce (*tamari*) and fish sauce (*nam pla*). In animal cells, however, polyamines also contribute to cell growth through eIF5A formation from spermidine, which is an essential protein for cell growth (*35*, *36*). The function of spermidine cannot be replaced by norspermidine for the formation of active eIF5A. Thus, we should keep in mind to ingest spermidine-rich food together with norspermidine-rich food.

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