9. The result of fecal examination in Yamanashi (4). (1964 ~ 1969)

Name region	Numbers	1964		1965		1966		1967		1968	1969
		Kato-katz	MIFC	Kato-katz	MIFC	Kato-katz	MIFC	Kato-katz	MIFC	MIFC	MIFC
KOFU	No.of sample	8426.0	1638	4416	1993	3666	1263	3827	1131	807	612
	Positive (%)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TAMAHO	No.of sample	—	692	—	310	—	308	—	700	529	37
	Positive (%)		0 (0.0)		0 (0.0)		1 (0.3)		0 (0.0)	0 (0.0)	0 (0.0)
RYUUOU	No.of sample	—	—	—	—	—	—	—	—	237	68
	Positive									11 (4.6)	4 (5.9)
SYOUWA	No.of sample	—	—	—	—	—	—	—	62	—	702
	Positive (%)								0 (0.0)		0 (0.0)
TATOMI	No.of sample	—	324	—	—	—	502	—	—	34	28
	Positive (%)		1 (0.3)				0 (0.0)			0 (0.0)	1 (3.6)
SHIKISHIMA	No.of sample	—	—	—	48	—	—	—	—	—	61
	Positive (%)				0 (0.0)						0 (0.0)
ISAWA	No.of sample	—	—	—	—	—	—	—	1160	—	66
	Positive (%)								0 (0.0)		0 (0.0)
ICHINOMIYA	No.of sample	—	—	—	—	491	—	—	—	—	35
	Positive (%)					0 (0.0)					0 (0.0)
MISAKA	No.of sample	—	—	—	—	—	—	—	—	—	43
	Positive (%)										0 (0.0)
YATSUSHIRO	No.of sample	—	—	—	—	—	—	—	—	—	31
	Positive (%)										0 (0.0)
SAKAIGAWA	No.of sample	—	—	—	—	—	—	—	—	—	54
	Positive (%)										0 (0.0)
NAKAMICHI	No.of sample	—	—	—	—	—	—	—	—	—	86
	Positive (%)										0 (0.0)
TOYOTOMI	No.of sample	—	—	—	—	—	—	—	—	—	11
	Positive (%)										0 (0.0)
MITAMA	No.of sample	—	—	—	—	—	—	—	—	—	21
	Positive (%)										0 (0.0)
HATTA	No.of sample	—	—	—	—	—	—	—	—	107	28
	Positive (%)									0 (0.0)	0 (0.0)
SHIRANE	No.of sample	—	—	—	—	—	—	—	—	89	21
	Positive (%)									0 (0.0)	0 (0.0)
KUSHIGATA	No.of sample	—	—	—	—	—	—	—	—	—	—
	Positive (%)										
WAKAKUSA	No.of sample	—	17	—	—	—	—	—	—	—	37
	Positive (%)		0 (0.0)								0 (0.0)
KOUSAI	No.of sample	—	—	—	—	—	—	—	—	—	51
	Positive (%)										0 (0.0)
MASUHO	No.of sample	—	—	—	—	—	—	—	—	—	—
	Positive (%)										
FUTABA	No.of sample	—	925	—	—	—	102	—	—	—	26
	Positive (%)		115 (12.4)				6 (5.9)				0 (0.0)
NIRASAKI	No.of sample	—	—	—	38	—	200	—	203	—	61
	Positive (%)				3 (7.9)		6 (3.0)		0 (0.0)		0 (0.0)
NAKATOMI	No.of sample	—	—	—	—	—	—	—	—	—	24
	Positive (%)										0 (0.0)
KASUGAI	No.of sample	—	—	—	—	—	—	—	—	—	19
	Positive (%)										0 (0.0)
YAMANASHI	No.of sample	—	—	—	—	—	—	—	—	—	—
	Positive (%)										

10. The result of fecal examination in Yamanashi (5). (1970 ~ 1979)

Name region	Numbers	1970		1971	1972-1975	1976	1978	1979
		Kat-kaz	MIFC	MIFC	MIFC	MIFC	MIFC	MIFC
KOUFU	No.of sample	1005	—	—	—	—	—	26
	Positive (%)	0 (0.0)						0 (0.0)
TAMAHO	No.of sample	—	256	32	6	—	—	8
	Positive (%)		0 (0.0)	0 (0.0)	0 (0.0)			0 (0.0)
RYUUOU	No.of sample	—	35	—	—	—	3	—
	Positive		1 (2.9)				0 (0.0)	
SYOUWA	No.of sample	467	233	731	8	1	—	—
	Positive (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
TATOMI	No.of sample	—	—	20	87	3	—	63
	Positive (%)			0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)
SHIKISHIMA	No.of sample	—	—	—	—	—	2	—
	Positive (%)						0 (0.0)	
ISAWA	No.of sample	1155	56	1711	—	—	—	62
	Positive (%)	0 (0.0)	0 (0.0)	0 (0.0)				0 (0.0)
ICHINOMIYA	No.of sample	—	—	—	—	—	—	10
	Positive (%)							0 (0.0)
MISAKA	No.of sample	—	—	—	—	—	—	20
	Positive (%)							0 (0.0)
YATSUSHIRO	No.of sample	—	—	—	—	—	—	16
	Positive (%)							0 (0.0)
SAKAIGAWA	No.of sample	—	—	—	—	—	—	36
	Positive (%)							0 (0.0)
NAKAMICHI	No.of sample	—	—	—	—	—	—	34
	Positive (%)							0 (0.0)
TOYOTOMI	No.of sample	—	—	—	—	—	—	—
	Positive (%)							
MITAMA	No.of sample	—	—	—	—	—	—	—
	Positive (%)							
HATTA	No.of sample	—	—	—	—	—	—	—
	Positive (%)							
SHIRANE	No.of sample	—	—	—	—	—	—	17
	Positive (%)							0 (0.0)
KUSHIGATA	No.of sample	—	—	—	—	—	—	—
	Positive (%)							
WAKAKUSA	No.of sample	—	—	—	25	1	—	40
	Positive (%)				0 (0.0)	0 (0.0)		0 (0.0)
KOUSAI	No.of sample	—	—	—	6	—	—	49
	Positive (%)				0 (0.0)			0 (0.0)
MASUHO	No.of sample	—	—	—	—	—	—	—
	Positive (%)							
FUTABA	No.of sample	—	—	—	—	—	—	—
	Positive (%)							
NIRASAKI	No.of sample	—	—	—	82	—	—	45
	Positive (%)				0 (0.0)			0 (0.0)
NAKATOMI	No.of sample	—	—	—	—	—	—	—
	Positive (%)							
KASUGAI	No.of sample	—	—	—	—	—	—	—
	Positive (%)							
YAMANASHI	No.of sample	—	—	—	—	—	—	—
	Positive (%)							

11. The result of ELISA test region in Yamanashi. (1958 ~ 1979)

Name region	Numbers	1958	1961	1976	1977	1978	1979
KOFU	No.of sample	593	—	—	239	242	730
	Positive (%)	76 (12.8)			0 (0.0)	0 (0.0)	0 (0.0)
TAMAHO	No.of sample	—	—	291	—	—	345
	Positive (%)			0 (0.0)			0 (0.0)
RYUUOU	No.of sample	—	—	—	—	672	—
	Positive					2 (0.3)	
SYOUWA	No.of sample	—	—	665	—	—	—
	Positive (%)			0 (0.0)			
TATOMI	No.of sample	—	—	733	—	—	1304
	Positive (%)			0 (0.0)			7 (0.5)
SHIKISHIMA	No.of sample	—	—	—	—	1680	—
	Positive (%)					0 (0.0)	
ISAWA	No.of sample	411	—	—	—	—	1551
	Positive (%)	108 (26.3)					9 (0.6)
ICHINOMIYA	No.of sample	—	—	—	—	—	841
	Positive (%)						2 (0.2)
MISAKA	No.of sample	—	—	—	—	—	1115
	Positive (%)						6 (0.5)
YATSUSHIRO	No.of sample	—	—	—	—	—	605
	Positive (%)						8 (1.3)
SAKAIGAWA	No.of sample	—	—	—	—	—	779
	Positive (%)						8 (1.0)
NAKAMICHI	No.of sample	—	—	—	—	—	928
	Positive (%)						0 (0.0)
TOYOTOMI	No.of sample	281	—	—	—	—	—
	Positive (%)	29 (10.3)					
MITAMA	No.of sample	—	—	—	—	—	—
	Positive (%)						
HATTA	No.of sample	—	—	—	—	—	—
	Positive (%)						
SHIRANE	No.of sample	—	—	—	—	—	709
	Positive (%)						5 (0.7)
KUSHIGATA	No.of sample	—	—	—	—	—	—
	Positive (%)						
WAKAKUSA	No.of sample	—	—	603	—	—	899
	Positive (%)			1 (0.2)			2 (0.2)
KOUSAI	No.of sample	—		—	—	—	1142
	Positive (%)						8 (0.7)
MASUHO	No.of sample	—	—	—	—	—	—
	Positive (%)						
FUTABA	No.of sample	1108	—	—	257	—	—
	Positive (%)	293 (26.4)			0 (0.0)		
NIRASAKI	No.of sample	2552	948	—	745	—	1531
	Positive (%)	504 (19.7)	321(33.9)		3 (0.4)		1 (0.1)
NAKATOMI	No.of sample	419	—	—	—	—	—
	Positive (%)	46 (11.0)					
KASUGAI	No.of sample	—	—	—	—	—	—
	Positive (%)						
YAMANASHI	No.of sample	—	—	—	—	—	—
	Positive (%)						

12. Surveillance of hepatosplenomegaly in the primary school children (1935)

Age	Male				Female			
	No. of subjects	Hepato-splenomegaly (%)	Egg (-) (%)	Egg (+) (%)*	No. of subjects	Hepato-splenomegaly (%)	Egg (-) (%)	Egg (+) (%)*
7	145	95 (65.5)	56 (38.6)	39 (26.9)	165	94 (57.0)	66 (40.0)	28 (17.0)
8	184	126 (68.5)	63 (34.2)	63 (34.2)	182	96 (52.8)	75 (41.2)	21 (11.5)
9	186	148 (79.6)	91 (48.9)	57 (30.7)	142	88 (62.0)	57 (40.1)	31 (21.8)
10	176	130 (73.9)	68 (38.6)	62 (35.2)	163	84 (51.5)	56 (34.4)	28 (17.2)
11	154	124 (80.5)	46 (29.9)	78 (50.7)	162	86 (53.1)	54 (33.3)	32 (19.8)
12	181	133 (73.5)	54 (29.8)	79 (43.7)	185	103 (55.7)	52 (28.1)	51 (27.6)
13	149	114 (76.5)	38 (25.5)	76 (51.0)	128	60 (46.9)	30 (23.4)	30 (23.4)
14	145	116 (80.0)	37 (25.5)	79 (54.5)	94	48 (51.1)	23 (24.5)	25 (26.6)
15	82	59 (72.0)	16 (19.5)	43 (52.4)	34	14 (41.2)	9 (26.5)	5 (14.7)
Total	**1402**	**1045 (74.5)**	**469 (33.5)**	**576 (41.1)**	**1255**	**673 (53.6)**	**422 (33.6)**	**251 (20.0)**

13. Surveillance of hepatosplenomegaly in the primary school children (1935)

Age	Male								Female							
	Endemic				Non endemic				Endemic				Non endemic			
	Subject	Height	Weight	Chest	Subject	Height	Weight	Chest	Subject	Height	Weight	Chest	Subject	Height	Weight	Chest
7	7199	106.9	17.4	54.2	1319	107.7	17.4	54.2	7486	105.8	16.5	52.6	1488	106.2	16.7	52.5
8	7274	111.5	19.1	56.1	1327	112.6	19.2	56.2	7611	110.6	18.3	54.4	1446	111.1	18.2	54.1
9	7250	116.2	20.9	58.0	1308	117.3	21.2	58.0	7579	115.1	20.1	56.1	1448	116.1	20.2	55.9
10	7309	120.5	22.6	59.4	1338	120.9	23.0	59.8	7441	119.7	22.1	57.9	1409	120.9	22.2	58.0
11	7047	124.6	24.8	61.6	1294	126.0	25.3	61.6	7181	124.2	24.3	59.8	1395	125.2	24.5	59.5
12	6951	128.9	27.0	63.5	1322	130.4	27.1	63.4	7098	129.2	27.0	62.4	1333	131.0	27.6	62.4
13	5546	133.1	29.4	65.3	1010	134.7	30.0	65.6	3116	134.2	30.4	64.8	421	135.6	31.1	65.2
14	4598	138.1	32.6	67.8	867	140.1	32.8	68.3	2284	139.6	34.6	68.8	291	141.1	34.8	68.5

14. Comparison of the stature between school children's development living in the endemic area and non endemic (1916 - 1930)

Age	Male								Female							
	Endemic				Non endemic				Endemic				Non endemic			
	Patients		Oshihara school Children		Yamanashi children		National avarage children		Patients		Oshihara school Children		Yamanashi children		National avarage children	
	Height	Weight	Height	Weight	Height	Weight	Height	Weight	Height	Weight	Height	Weight	Height	Weight	Height	Weight
6	105.7	17.3	108.7	18.6	108.2	18.2	108.6	18.5	104.2	16.9	102.3	16.9	106.9	17.7	107.7	17.9
7	110.3	17.9	118.7	19.9	113.0	20.2	113.4	20.3	108.9	17.3	110.7	19.3	111.8	19.1	112.7	19.6
8	116.2	22.3	121.4	22.5	117.6	21.6	118.1	22.3	115.8	21.8	111.7	20.4	116.3	20.9	117.3	21.5
9	116.4	22.4	122.3	24.5	122.4	23.5	122.4	24.2	116.2	21.6	121.1	22.9	120.9	22.8	121.7	23.6
10	122.1	24.7	123.5	25.7	125.6	25.7	126.5	26.4	121.8	24.2	124.6	25.1	125.2	24.9	126.8	25.8
11	127.8	25.4	130.5	27.4	129.9	27.7	130.7	28.8	128.3	25.7	125.5	28.4	130.2	27.2	131.0	28.5

15. Comparison of the stature between school children's height and weight living in the endemic area and non endemic (1950)

Age	Male						Female					
	Healthy Children (n=4550)			Patients (n=110)			Healthy Children (n=4577)			Patients (n=53)		
	Height	Weight	Chest	Height	Weight	Chest	Height	Weight	Chest	Height	Weight	Chest
6	110.0	18.4	55.9	107.0	17.5	53.7	109.2	18.0	54.7	110.0	19.8	56.0
7	117.5	20.3	58.3	117.4	20.1	59.8	114.3	18.8	56.5	111.5	17.5	53.2
8	119.7	22.0	60.3	118.0	20.1	58.6	119.4	21.9	58.5	119.7	21.7	57.5
9	124.4	24.9	63.1	122.0	24.1	62.3	124.2	24.9	60.7	124.1	24.1	59.2
10	135.5	26.3	64.6	127.9	26.3	58.6	128.7	26.1	63.4	127.7	26.0	59.1
11	133.7	28.4	65.0	133.0	28.5	64.6	132.3	29.3	64.4	134.4	29.2	64.4
Average	125.1	23.4	62.3	120.8	22.2	59.5	122.6	23.2	59.5	121.5	23.2	58.3

16. The case of animal infection with Schistsome.

Animals	1904			1925 - 1927			1929			1933～34		
	No of examin.	positive	%	No of examin.	positive	%	No of examin.	positive	%	No of examin.	positive	%
Dog	2	0	0	2	1	50						
Cat	9	9	100									
Mouse												
Cattle						9.1	30	6*	20	1203	468	38.9
Rabbit				22	2							
Mole												
Note	Fujiro Katsurada (1904) Iwaho tsuchiya 1904 1904 July to August by dissection			Outbrake of the situation of Schistosomiasis in Yamanashi (1928) Results of 9 town and 16 points.			June 18, 1929; reported Yamanashi daily news Minami Saitoh (1930)			Minami Saitoh (1935)		

Cat had lived in Ookamata(2), Ikeda, Satogaki, mutsugugawa, Arakawa, Iinuma, Aikawa, those in 6 cats were detcted Adult worm.

Animals	1940			1944			1945			1950		
	No of examin.	positive	%	No of examin.	positive	%	No of examin.	positive	%	No of examin.	positive	%
Dog				51	12	23.5	353	176	50	64	39	60.9
Mouse	1707	656	36.7				1707	656	36.7			
Cattle	2	2	100.0	377	187	49.6	7059	2184	30.8	1271	308	24.2
House	44	309	68.2	5612	1964	35	967	0	0			
Goat				208	0	0	1118	158	14.1			
Weasel	10	9	90.0	838	16	1.9	10	9	90			
Mole	68	13	19.0				68	13	19			
Note	Tasuo Kato 'The history of the research on schistosomilasis japonica in Yamanashi and its control project (1940) Result were obtained by autopsy			Outbrake of the situation of Schistosomiasis in Yamanashi (1953)			Repoeted number processed to the examination of GHQ (General Head Quarter)			Cattle: Agiricultural office record Dogs: Fecal examination		

Animals	1940			1944			1945			1950		
	No of examin.	positive	%	No of examin.	positive	%	No of examin.	positive	%	No of examin.	positive	%
Dog	462	118	25.5	6838, 0	3427	5. 00.	208	0	0	35	0	0
Mouse	68	2	2.9				183	31	16.9	354	*2	0.56
Cattle	2530	78	3				1624	0	0			
Weasel							1	1	100			
Mole							2	0	0			
Note	Dogs: Y. Hosaka et al. 1955 Rats data were obtained by autopsy. Cattle was examined by scraping the mucous membrane			Dogs: Iijima(1963) Cattle; Agricultural office records(1935 -40)			Dogs: Kuzumi (1971) Cattle; Agricultural office records(1941 -42)			* indicates Usui- pond		

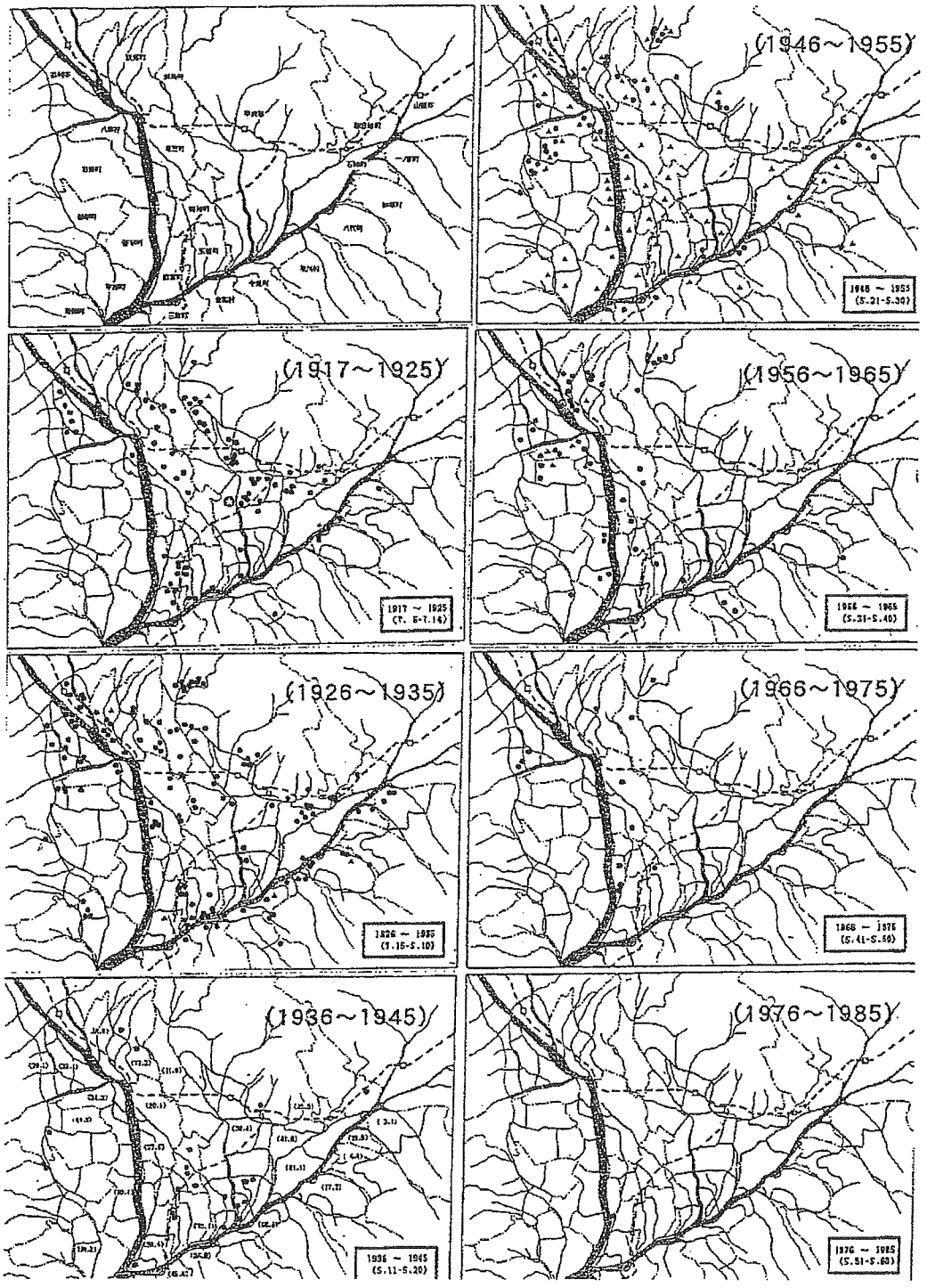
17. Fecal examination of domestic cattle and treatment.

Year	No. of examin	Egg positive	%	No. of treatment
1943	377	187	49.6	
1944	5612	1964	35.0	1785
1945	3238	1124	34.7	709
1946	1537	476	31.0	0
1947	810	384	47.4	146
1948	819	180	22.0	26
1949	1491	163	10.9	86
1950	1271	508	24.2	215
1951	3804	257	6.8	187
1952	3851	223	5.8	135
1953	3633	15.1	4.2	94
1954	2530	78	3.0	57
1955	2725	66	2.4	66
1956	2492	70	2.8	47
1957	1544	28	1.8	28
1958	2032	20	0.9	20
1959	2052	13	0.6	13
1960	1683	13	0.7	13
1961	1473	4	0.2	4
1962	1341	6	0.4	6
1963	1461	3	0.2	3
1964	1172	1	0.1	1
1965	932	0	0.0	0
1966	1097	0	0.0	0
1967	545	0	0.0	0

Year	CATTLE	HORSE
1915	2324	17564
1920	1640	17295
1924	1792	17218
1925	1882	15682
1935	1723	14100
1940	—	—
1943	10801	13356
1945	10995	13432
1950	11650	12707
1955	18673	8561
1960	20135	3966
1965	14098	960
1970	12812	257

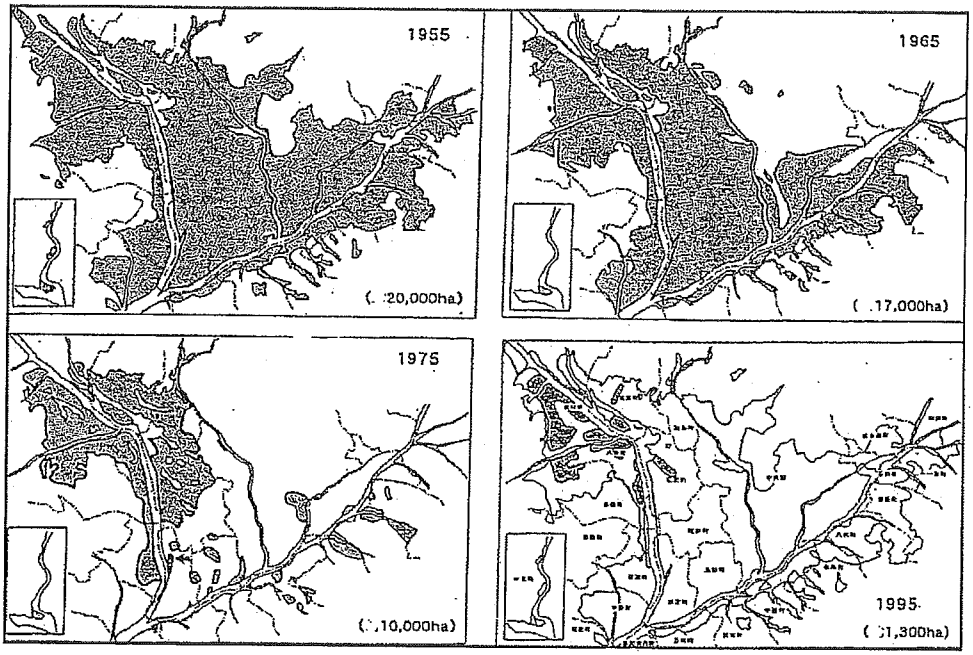
Fecal examination: 1944 to 1949, Kato-katz method.
After 1950, Direct curettage of recum mucous membrane methods.
Treatment: 1944 to 1946
Reference; 1944 to 1951, 1952 to 1956

18. Annual record of Miyairi snail habitation (1917 - 1985)

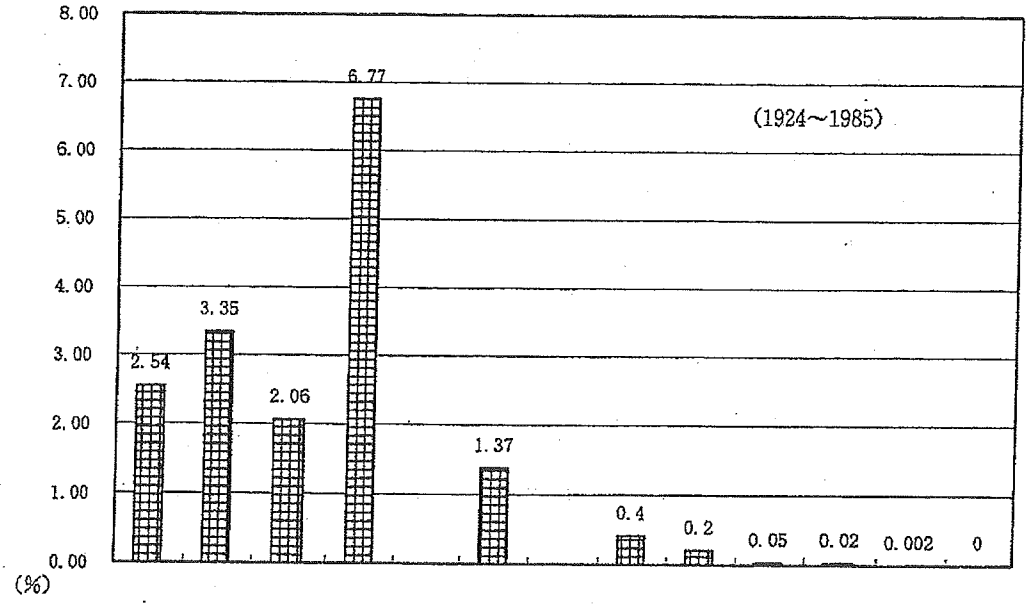


● Point of Miyairi snail habitation.
▲ Report of Miyairi snail habitation.

19. Annual record of Miyairi snail habitation (1917 - 1985)



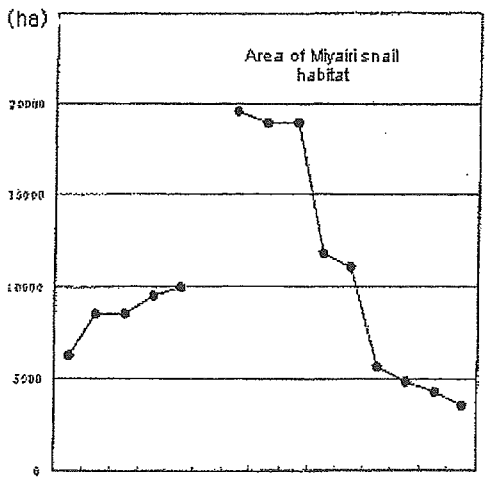
20. Annual record of infection rate of Muyairi snail.



21. Annual record of Miyairi Snail habitation

	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996
KOFU	41.3	41.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
TAMAHO	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
SYOWA	27.9	33.9	42.9	15.1	28.1	25.7	30.7	30.7	21.1	15.1	8.2
TATOMI	10.8	10.8	10.8	10.8	23.9	42.4	10.8	10.8	0.0	0.0	0.0
RYUUOU	242.0	286.7	254.4	276.9	266.3	288.8	305.2	66.2	68.3	56.7	39.8
SHIKISHIMA	109.4	106.6	118.8	80.0	49.0	5.5	43.5	41.6	39.5	43.8	20.0
MITAMA											
ISAWA	0.0	0.0	0.0	0.0	0.0	0.0	0.0				
ICHINOMIYA											
MISAKA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
YATUSHIRO	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
SAKAIGAWA	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
NAKAMICHI	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0		
TOYOTOMI											
HATTA	289.1	297.2	331.1	258.8	292.1	280.8	349.4	322.1	360.9	297.6	186.6
SHIRANE	236.8	231.1	207.9	187.1	241.6	234.1	268.9	268.9	269.4	268.9	139.1
KUSHIGATA											
WAKAKUSA	149.0	126.2	162.9	162.9	140.5	135.6	126.6	130.7	130.7	120.8	115.2
KOUSAI											
MASUHO											
FUTABA	85.7	86.4	117.7	80.8	44.0	43.5	44.0	32.0	14.0	41.1	4.6
NIRASAKI	464.9	466.2	470.6	470.8	418.9	313.4	396.5	424.8	335.4	393.3	391.4
KASUGAI											
YAMANASHI											
NAKATOMI	55.6	554.0	62.4	58.8	59.4	60.4	62.4	63.0	63.0	63.0	58.1
ICHIKAWADAIMONN											
TOTAL	**1712.5**	**1741.8**	**1779.6**	**1602.0**	**1593.8**	**1430.2**	**1638.1**	**1390.8**	**1302.3**	**1288.4**	**963.0**

Snail habitation area: Total area size of the snail habitation in each region was sum of the reported until where the snails were found. Basically the area size of the endemic area and the snail habitation are the same. However, the endemic area needed to process the steps to declare disease free, the area since of the endemic area was bugger than that of the snail habitation.



22. Amount of using Quicklime used for molluscicide

Present city	Previous City	Implementation area (TANN)	Ditch extention (KEN)	Ridge extention (KEN)	Amount of Quicklime (HYOU)	No. of workers	Period	Not implementation area (3300㎡)
KOFU	KOFU	967	161871	384055	106108	14909	1925 - 26, 31 - 38	0
	TAMAO	304	47128	29498	46800	2865	1925 - 27, 30 - 38	17
	YAMASHIRO	170	29785	39575	14659	2762	1937 - 38	25
	KOUUNN	126	29653	15162	25453	1775	1925 -26, 30 - 38	0
	TIZUKA	170	25016	40560	11278	1406	1925 - 33	0
	OOMIYA	86	6493	29434	9761	695	1929 - 31	0
	SUMIYOSHI	238	30404	43715	15032	2355	1937 -38	0
	ASAI	35	4106	8100	2302	362	1938	45
	CHIYODA	4	280	480	75	14	1938	0
	IKEDA	180	27777	89859	28990	2804	1929 - 23	0
	OOKAMADA	100	23352	5072	11287	2208	1938	99
	FUTAKAWA	35	4860	13125	2864	439	1938	85
TAMAHO	INAZUMI	76	13212	20839	6388	874	1938	209
	SANNCYOU							249
SYOUWA	SAIJYOU	331	78037	189114	42256	7568	1937 - 38	20
	JYOUSUI	177	24733	66557	13933	1982	1937 - 38	28
TATOMI	OIKAWA	50	7870	17425	3640	624	1938	40
	HANAWA, SHINOBU							278
RYUUOU	RYUUOU	505	74353	190304	62287	7541	1929 - 38	0
	TAMAHATA	285	50803	99726	30277	4014	1931 - 38	0
SHIKISHIMA	SHIKISHIMA	336	35006	84369	33811	3323	1927 - 31	0
	MUTUZAWA	24	1731	8541	2749	320	1927 - 30	0
	YOSHIZAWA	32	2190	11303	3517	382	1926 - 27, 30	0
KASUGAI	KASUGAI	77	5316	797	4002	327	1926	0
	OKABE	159	18876	6012	13546	818	1926 - 27, 30	0
ISAWA	ISAWA	42	9326	12575	5945	798	1927 - 30, 32 - 33	0
	HANABUSA	186	33048	47705	23599	2235	1928, 30 - 31	0
	FUJIMI	175	19276	23513	10398	987	1929 - 30, 34	0
ICHINOMIYA		130	10502	12575	12929	798	1926, 28 -30	0
MISAKA	NISHIKI	87	13859	27422	9075	1401	1929 - 31	0
	KINNSYOU	8	1260	2110	450	94	1936	0
	KACYOU	10	910	2425	500	118	1937	0
YATSUSHIRO	KITAYATSUSHIRO	71	18608	28450	8355	1094	1933 -34	0
	MINAMI YATSUSHIRO	90	14361	26878	8750	916	1933	0
	NAGAI	5	314	1250	350	48	1937	0
	KOUKE	15	1770	2200	550	124	1938	0
	YONEKURA	5	730	1350	350	80	1938	0
	MASUDA	49	10840	13151	4818	601	1922 - 34	0
SAKAIGAWA	SAKAIGAWA	120	24421	59136	12605	1779	1934 -36	0
NAKAMICHI	SIRAIKAWAHARA	41	6839	4302	2855	361	1929, 1934	0
	KAMISONE	85	11592	28084	6.52	983	1934 - 35	0
	SHIMOSONE	45	6247	10971	2643	408	1935 - 36	0
	YUSAGUCHI	87	10605	36510	7555	1689	1935 - 37	0
TOYOTOMI	TOYOTOMI	108	11873	49015	9530	1299	1933 - 36	0
MITAMA	OOTSUKA	75	6555	3040	2505	370	1933	0
HATTA	MIKAGE	230	32216	88294	21838	3758	1933 - 38	10
	TANOOKA	65	16891	12195	6500	984	1936, 38	34
SHIRANE	MINAMOTO	80	2960	16995	3698	562	1935 - 36	0
	IINO	20	1968	2088	1015	161	1938	0
	MOMOTA	78	10080	21330	3534	800	1934 - 1936	0
	IMASUWA	58	23205	31960	9191	1239	1936 - 37	2
WAKAMUSA	NIBANN	11	1190	2130	5.6	80	1035 -36	0
	KAGAMINAKAJYOU	101	28612	38812	9754	1153	1037 - 38	0
	FUJITA	55	3460	4851	1639	226	1935 - 36	0
KASAI	OCHIAI	4	520	560	200	40	1935	0
	OOI	8	1665	1960	650	99	1936	0
	GOMYOU	156	16265	25300	8765	1199	1932 - 36	0
	NANNGO	199	20321	43230	10436	1652	1934 - 38	0
MASUHO	MASUHO	18	1660	630	660	101	1934	0
FUTABA	TOMI	215	36901	119259	40544	3723	1927 - 30	0
	SIOZAKI	365	55916	167359	54621	7027	1932 - 33	0
NIRASAKI	NIRASAKI	122	19406	37623	9373	1651	1928 - 37	20
	SEITETSU	20	2138	1888	765	225	1934 - 35, 37 -38	0
	KAMIYAMA	50	9288	3163	4.956	472	1938	0
	ASAHI	193	29245	61807	27808	2351	1927, 30	0
	OOKUSA	145	28363	61295	25329	2765	1927 - 29,31	0
	TATSUOKA	173	32025	105301	32802	3800	1928 - 31, 33 - 35	0
KUSHIGATA	SAKAKI						-	10
ALL TOTAL		8287	1292083	2645380	895937	1106180		1171

Reference:Tatsuya Kato, Resarch and prebention of Schistosomiasis japonica in Yamanashi, 1940
The table was used unit, 1 TAN:3300㎡, 1 KEN: 180m, 1 HYOU: 21kg

23. Amount of using Quicklime used for molluscicide

Year	Enterprise	molluscicide No. of town	Area (CHOU)	Ridge extention (KENN)	Ridge extention (KENN)	Area of farm (UNE)	Amount of Calcium cyanamide (BAG)	Amount of Carbide (CAN)	Total no. of workers (PERSONS)
1944 - 1948	Prefectural	1-53	11996	2076898	1809750	29083	57558	3027	128561
1948	Village-run	1-51	8875	549857	444129	12211	11495	-	27907
1949	Village-run	1-25	3928	683296	536115	-	15715	-	43333
1950	Village-run	1-51	?	1585827	1246553	156623	52743	8	74721
1951	Village-run	1-58	4467	923992	666061	1213	26212	50	47711
TOTAL			**29266**	**5819870**	**4702608**	**199130**	**163723**	**3085**	**322233**

24. Amount of kerosene for molluscicide in the year

Unit: 1 litter

YEAR	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983
KOFU	1665	375	180		450	1922	2125	3220	1100	396	570	648	144	630
TAMAHO				4800	6200	10000	1290	4300	4000	1362	1725	1000	1133	1429
SYOUWA				1500	4800	8100	4200	12821	10812	2800	2439	2381	1935	1807
TATOMI				9382	250	5000	5000	8268	220	2741	1538	1329	900	480
RYUUOU				600	400	5100	5458	2520	1700	1885	1800	1200	1798	2070
SHIKISHIMA	450	2135	3998	3805	2365	3829	2961	7939	4550	5897	4976	3650	3760	4353
ISAWA						54		36						72
ITINOMIYA						142	100							
MISAKA					50	18		730						27
YATUSHIRO	20			150	18	400		1000	600	418	400	40		60
SAKAIGAWA								482		200				
NAKAMICHI				2	980		200			180	40			
TOYOTOMI				72										
MITAMA														
HATTA				4000	6300	3777	2800	5942	4628	4187	1580	310	1500	1112
SHIRANE				6400	5429	2497	1509	3285	3450	2377	1203	942	167	563
KUSHIGATA														
WAKAKUSA			450	1200	350	200	14990	16000	4700	2716	800		90	1127
KOUSAI														
MASUHO														
FUTABA			1386	20		3553	5200	5234	5712	2248	1095	1618	400	
NIRASAKI				11980	4636	9692	7300	10360	7030	5655	330	310	3873	330
KASUGAI														
YAMANASHI														
ICHIKAWADAIMONN														
NAKATOMI			120	120	520	340	1220	2370	1700	3150	1420	959	1765	1830
TOTAL	2135	2510	6014	43911	32228	54284	53133	82137	48502	33062	18496	13428	15699	14061

Reference;The war against regional disease (1977)

25. Amount of Santbrite and PCP (1953 - 1957)

Presenc City	Previous town	1953 Sant bright (Spring)	1954 Sant bright (Spring)	1954 Na-PCP (Autumn)	1955 Na-PCP (Spring)	1955 Na-PCP (Autumn)	1956 Na-PCP (Spring)	1956 Na-PCP (Autumn)	1957 Na-PCP (Spring)
KOFU	OTHER AREA	300.45	1055	360					
	YAMASHIRO		264	25					
	SUMIYOSHI		295	35					
	ASAI		209	15					
	TAMAO		167	25					
	CHIYODA		-8	5					
	OOKAMADA		536	50					
	FUTAGAWA		321	25					
	KOUUNN		173	25					
	TOTAL		**3028**	**555**	**2915**	**395**	**1800**	**2550**	**3410**
TAMAHO	INAZUMI		625	100					
	SANCYOU		448	100*					
	TOTAL		**1073**	**100**	**1060**	**	**910**	**369**	**855**
SYOUWA	SYOUWA		770	92	758	100	1195	382	1120
TATOMI	TATOMI		636	100	626	85	500	80	480
RYUUOU	RYUUOU		603	160	595	80	825	130	
	TAMAHATA	303.88	431	75	425	60	510	148	
	TOTAL	**303.88**	**1034**	**225**	**1020**	**140**	**1335**	**278**	**1250**
SHIKISHIMA	SHIKISHIMA		565	*					
	MUTSUZAWA	16.5	181	*					
	YOSHIZAWA	21.74	146	*					
	TOTAL	**38.24**	**892**		**840**	**110**	**490**	**80**	**460**
ISAWA	ISAWA		200	35	187	25	205	30	680
	HAYABUSA		277	*	274	37	350	170	
	FUJIMI	115.52	155	30	148	20	380	60	360
	TOTAL	**115.52**	**632**	**65**	**609**	**82**	**935**	**260**	**1040**
ITINOMIYA	ICHINOMIYA		176	35	172	25	350	90	330
MISAKA	KINSEI	80.17	108	15					
	KACYOU		3	3					
	TOTAL	**80.17**	**111**	**28**	**92**	**15**	**160**	**25**	**235**
YATSUSHIRO	YATSUSHIRO		440	25	436	60	400		
	GOSYO		14	*	13	10	45		
	TOTAL		**454**	**25**	**449**	**70**	**445**	**75**	**420**
SAKAIGAWA	SAKAIGAWA		188	25	186	30	200	35	190
NAKAMICHI	KASHIWA		103	25					
	YUSAGUCHI		128	25					
	TOTAL		**231**	**50**	**227**	**30**	**375**	**60**	**356**
TOYOTOMI	TOYOTOMI	380.07	263	50	261	35	250	40	235
MITAMA			267	15	248	30	160	25	150
HAATA	MIKAGE	554.36	376	75	366	50	430		
	TANOUCHI	277.89	191	50	183	25	200		
	TOTAL	**832.25**	**567**	**125**	**549**	**75**	**630**	**110**	**595**
SHIRANE	MOMOTA		102						
	IMASUWA	369.54	251	50					
	KOMA		21						
	SHIRANE				335	50	280	65	260
	MINAMOTO	101.01	66	*	61	10	110	70	110
	TOTAL	**470.55**	**440**	**50**	**396**	**60**	**390**	**135**	**370**
KUSHIGATA	SAKAKI		52	5	50	10	20	10	20
WAKAKUSA	SANNKEI		16						
	KAGAMINAKAJYOU	563.15	454	*					
	FUJITA		68						
	TOTAL	**563.15**	**538**		**435**	**60**	**625**	**285**	**585**
KOUSAI	GOMYOU		203	10					
	NANNGO		223	50					
	OOI		21	5					
	OCHIAI		4	5					
	TOTAL		**451**	**70**	**526**	**70**	**625**	**100**	**585**
MASUHO	MASUHO		14	5	13	10	30	10	30
FUTABA	TOMI	510.28	348	60					
	SHIOZAKI	598.19	469	40					
	TOTAL	**1108.47**	**817**	**100**	**796**	**100**	**835**	**150**	**780**
NIRASAKI	NIRASAKI	196.88	265	35					
	FUJII		12	5					
	SEITETSU		77	8					
	KAMIYAMA		100	12					
	ASAHI	136.28	382	60					
	OOKUSA	175.6	614	70					
	TATSUOKA	581.47	802	80					
	TOTAL	**1090.23**	**2252**	**270**	**2193**	**290**	**1360**	**210**	**1275**
KASUGAI	OKABE		137	*	133	10	265	174	
	KASUGAI		3	10	32	10	50	48	
	TOTAL		**140**	**10**	**165**	**20**	**315**	**222**	**125**
NAKATOMI					110	43	160	60	55
YAMANASHI	HIKAWA		41	*	41	10	50	15	50
TOTAL		**5283**	**15067**	**2000**	**14737**	**1895**	**14145**	**5656**	**15000**

26. Amount of molluscicide in the year

	1965		1966	1967	1968		1969		1970		1971	1972	1973	1974	1975	1976		1977	1978	1979	1980		1981		1982	1983
	PCP	Yulimin	PCP	PCP	PCP	Yulimin	PCP	Yulimin	PCP	Yulimin	PCP	Yulimin	Yulimin	Yulimin	Yulimin	Yulimin	B-2 tab.	B-2 tab.	B-2 tab.	B-2 tab.	B-2 tab.	B-2 liq.	B-2 tab.	B-2 liq.	B-2 liq.	B-2 liq.
KOFU	800	50	700	700	800	250	800	50	100	600		1000	1000	600	600	1320	800	800	1580	1300	1300	740	300		3320	260	260
TAMAHO	300		200	200	220	50	60	140		450		200	200	200	200	400	250	300	400	400	400	270	76		200	75	20
SYOUWA	500		260	120	100	10	30	50	20	80	60	120	280	200	200	400	150	200	500	700	840	420	248		500	404	400
TATOMI	200		100	60	50			230		350		200	200	200	200	500	300	700	2110	1000	700	50	88		96	45	30
RYUIJOU	2000	300	3280	3000	3240	700	440	2280	750	3000	2350	3500	7000	5000	5000	5000	2240	2040	1200	1200	1200	800	350		655	600	700
SHIKISHIMA	800	50	880	960	1200	550	2000	2170	1000	2500	1000	1200	2000	1000	1000	1000	600	600	1550	1200	1200	900	180	1240	48	758	750
ISAWA	100					20	20	20		20		30	25	20		10	10	10	30	30	40	40					35
ICHINOMIYA	100		50	20	60	20	40	80	20	40		5	100	20	20	20	10	10	20	20	20				6		
MISAKA	300		100	100	60	5	50	120	100	290		300	500	300	300	300	200	100	250	200	90	70	17		20	40	40
YATSUSHIRO	300		200	100	30	5	20	60		100		300	220	60	60	60	40	20	60	80	80	150	35	20	112	80	80
SAKAIGAWA	100		50	50	10			30		20		50	17	20	20	10	10	10	30	60	60	50	10		21	80	
NAKAMICHI	950		300	140	20	20	80	200	20	140		100	240	160	160	160	80	60	200	130	160	120	20		80	30	30
TOYOTOMI	50		50	20	20			70		50		30		30	20	20	10	10	20								
MITAMA	100		50	20	30						20		20	20													
HATTA	1700	300	2800	3000	3000	300	2000	1250	500	4250	670	4300	5198	3400	3400	4000	2500	1440	3500	3500	2800	1500	620		500	550	600
SHIRANE	1610	200	2000	1920	2000	500	1500	1200	1000	2500	1000	2000	3000	2000	1000	1500	800	260	1000	1200	1400	740	435		957	778	1000
KUSHIGATA																											
WAKAKUSA	900	200	2400	2700	12500	300	1800	700	300	1200	300	230	1100	1000	1000	1400	600	300	1500	2000	3000	1660	792		1410	1000	700
KOUSAI				20																							
MASUHO																											
FUTABA	1700	200	1700	1700	1500	300	740	1070	530	1560	500	1560	1700	1600	1600	1600	1000	900	2150	2000	2000	1100	600		1560	1962	
NIRASAKI	3500	300	4400	4630	4600	800	2750	3500	1400	3870	1920	6535	7400	5000	6000	7080	3980	3913	8800	8000	8000	4500	2004		4800	4283	4100
NAKATOMI	200		580	500	500	200	400	600	510	600	600	600	600	300	120	180	60	20	140	360	550	240	260	60	400	560	600
KASUGAI																											
YAMANASHI																											
ICHIKAWADAIMONN														30	30	20	20	40	40								
TOTAL	16210	1600	20100	19960	19940	4030	12730	13620	6250	21820	8420	22260	30800	21130	20930	24990	13660	11713	25080	23420	23940	13150	6035	1320	14685	11495	9345

Unit: PCP, Yulimin, B-2 Tablet: kg; B-2 Liquit: 500ml
Cost: B-2 Tablet: ¥680 (1979), ¥710 (1980), ¥740 (1981)

27. Concrete irrigation canal extension

PLACE	1950 - 1956		1957 - 1973		1974	1975	1976	1977	1978	1979	1980	1974 - 1980		TOTAL 1950 - 1980	
	Ditch extention (m)	TOTAL EXPENSES	Ditch extention (m)	TOTAL EXPENSES	Ditch extention (m)	Ditch extention (m)	Ditch extentio n (m)	Ditch extention (m)	Ditch extention (m)	Ditch extention (m)	Ditch extentio n (m)	Ditch extentio n (m)	TOTAL EXPENSES	Ridge extention (KENN)	TOTAL EXPENSES
KOFU	23575	24984738	157509	408591998	2784	4242	4812	6864	18887	8826	7604	54019	1109322664	233.103	1542899400
TAMAHO	7229	7983510	91473	219169977	1911	1842	2053	2874	4736	2400	1393	17209	475214094	115911	702367581
SYOWA	7427	8230800	89143	213579521	1192	1099	759	3507	3450	4197	2.639	16843	358835940	113413	580646261
TATOMI	8370	8839038	51430	138206486	1740	2244	2328	4719	4465	3103	2244	20843	507663150	80643	654708674
RYUOU	9952	12577138	142343	365813400	3152	5427	7419	4908	3649	870	2303	27728	315201492	180023	693592030
SHIKISHIMA	6752	7187608	38629	97531785	1843	2166	2714	2365	2086	1856	2038	15068	176115257	60.449	280834650
MITAMA	4607	5066200	24938	60301307										29545	65367507
ISAWA	9709	10062319	69844	148971638	1355	1958	1509	1976	2600	6065	6420	21883	296335455	101436	455369412
ICHINOMIYA	3480	3509649	15760	31494616	419	222	163	473	613	607	674	3171	44049838	22411	79054103
MISAKA	4092	3347797	36528	70579662	301	1413	1310	1247	504	82		4857	39677671	45477	113605130
YATSUSHIRO	6090	5656507	25128	38421266	1093	864	879	1350	3019	2202	2023	11430	155828171	42648	199905944
SAKAIGAWA	3006	2653039	33752	60899486	183	222	350	298	361	595	420	2429	66845129	39187	130197654
NAKAMICHI	3847	4034637	60293	118357336	893	895	404	955	826	1026	1064	6063	71823652	70203	194215625
TOYOTOMI	3019	3311260	37204	61005205										40223	64316465
HATTA	13045	10216797	98575	152259306	800	1194	895	1601	1214	1380	976	8080	211934368	119680	374410471
SHIRANE	14031	11899537	110202	166802389	1180	1377	861	1465	1361	914	705	7863	150640069	132096	329341995
KUSHIGATA	1230	938599	1394	1081900										2624	2065499
WAKAKUSA	6956	7492189	72170	185453819	1395	2495	1017	2244	2759	1.116	1227	12253	274544047	91379	467490055
KOUSAI	8.751	9887310	122270	251303.522	877	706	548	1.168	921	771		4991	148913.128	136.012	410103960
MASUHO	1147	1154239	2326	2598343										3473	3752582
FUTABA	10671	10959.054	75769	127096356	1236	2040	2224	1756	2607	1286	1145	12294	214731988	98734	352787398
NIRASAKI	24062	23284615	189361	390559910	5457	8203	8264	4804	3172	2201	2611	34712	391276173	248135	805120698
KASUGAI	4260	3982062	18311	27479064										22571	31461126
YAMANASHI	1601	1529574	9835	25803644										11436	27333218
NAKATOMI	1456	999259	10898	15136812										12354	16136071
TOTAL	186365	189832475	1585085	2969906750	27811	38609	38509	44574	57230	39497	35486	281716	5008752286	2053166	8168491511

28. Concrete irrigation canal extension and total expenses.

	1981	1982	1981- 1982		1983	1984	1985	1983 - 1985		All Total 1981 - 1985	
	Ditch extention (m)	Ditch extention (m)	Ditch extention (m)	TOTAL EXPENSES	Ditch extention (m)	Ditch extention (m)	Ditch extention (m)	Ditch extention (m)	Ditch extention (m)	Ditch extention (m)	TOTAL EXPENSES
KOFU	3840		3840	90509700	631	571	740	1942	85952820	5782	176462520
TAMAHO	1703	33	1736	36408686	458	713		1171	24413000	2907	60821686
SYOUWA	2962	1881	4843	98812130	623	663	513	1799	39032825	6642	137844955
TATOMI	4275	5355	9630	204810253	1188	1230	1354	3772	93760759	13402	298571012
RYUUOU	5691	3252	8943	197192740	1139	1282	1089	3510	89897892	12453	287090632
SHIKISHIMA	2431	3081	5512	95665760	805	517	836	2158	46208500	7670	141874260
MITAMA											
ISAWA	1785	714	2499	55115114	592	723	752	2067	46335950	4566	101451064
ICHINOMIYA	219		219	4831040						219	4831040
MISAKA	134		134	1690890	60		158	218	4350000	352	6040890
YATSUSHIRO	4674	2755	7429	132635037	472	658	813	1943	38069897	9372	170904934
SAKAIGAWA	2567	1247	3814	51920365						3814	51920365
NAKAMICHI	1738	1480	3218	46477000	800	54	2	273	411456		
TOYITOMI										5954	87891556
HATTA	1686	3040	4726	77942821	1119	955	884	2958	45084950	7684	123027771
SHIRANE	2013	3240	5253	76719081	527	617	961	2105	36502718	7358	113221799
KUSHIGATA											
WAKAKUSA	1543	726	2269	51369201	982	770	917	2669	59061750	4938	110430951
KOUSAI	423		423	8860973						423	8860973
MASUHO											
FUTABA	4427	4616	9043	161699063	682	646	595	1923	36634730	10966	198333793
NIRASAKI	4863	2247	7110	97164850	704	878	1180	2762	53682520	9872	
KASUGAI											150847370
YAMANASHI											
NAKATOMI	639	81	720	9316980	522	522	412	1456	18030000	2176	27346980
TOTAL	47613	33748	81361	1499341684	11304	11799	12086	35189	758432867	116550	2257774551

29.Use of a preventive ointment for ceraria infection.

	1954		1955		1956		1957	1961	1962	1963	1964	1969	1970	1971	1972	1973
	Tubes	Persons	Tubes	Persons	Tubes	Persons										
KOFU			440	880		960	1680	1680	1680	1680	168		200			
TAMAHO	257	514	157	314		460	560	308	79	140	23	56	116	360	1500	
SYOUWA	379	758	70	140		303	560	415	112	280	104					
TATOMI	50	100				40	280	336	224		15					
RYUUOU	500	1000	207	414		138	1104	1120	1120	840	392					
SHIKISHIMA	110	220	20	40		56		381	536	560	560					
MITAMA							34	118								
ISAWA	43	86	13	26		40										
MISAKA							135									
YATSUSHIRO							881									
NAKAMITI			100	200		150										
TOYOTOMI			41	82		100										
HATTA	802	1604	359	718		285	1960	2240	2240	2240	1680	560	2160	2400	900	
SHIRANE	310	620	316	632		557	2800	2800	2240	1748	2264	2240	3816	3840	1530	
WAKAKUSA	350	700	500	1000		300	555	560	840	1080	1288	1400	1800	1600	1050	1050
KOUSAI	231	462	1121	2242		1860	1960	1960	1960	560	784					
FUTABA	1248	2496	500	1000		410	1266	1400	1464	1636	106	1680	2880	2000	600	900
NIRASAKI	394	788	638	1276		1000	2128	1540	1040	1980	1182	3600	4810	2400	1050	
NAKATOMI						660	588	852	532	560	269	1120	880	800	750	
TOTAL	4674	9348	4482	8964	3555	7319	16491	15710	14067	13304	8835	10656	13400	7380	5805	5805

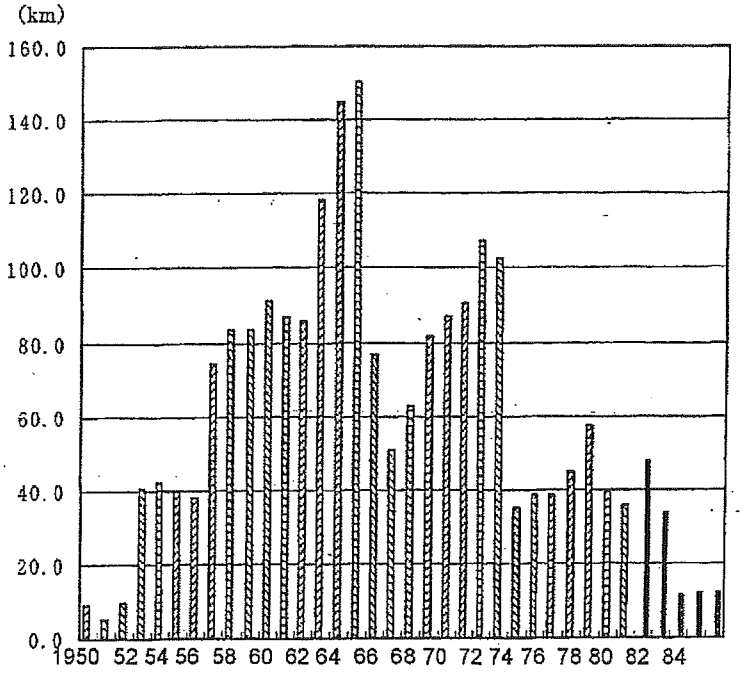
Reference: 1954 - 56 ; Report of Institute of Health And Environmental Science, 1960 - 1973 : The war against regional disease (1977)

In 1951 Bentrate (Benzyl bennzoate, Dibutbylpbtalate), BD (Dimetbylphtalate alone) were used.

Now, In 1955 - 1956 almost in village were used.

30. Annual record of the extension of construction

Year	Extention construction	Extention re-construction
1950	9	
1951	5.4	
1952	9.7	
1953	40.2	
1954	42.9	
1955	39.9	
1956	38.2	
1957	74.5	
1958	83.4	
1959	83.2	
1960	91.1	
1961	86.8	
1962	86	
1963	118.2	
1964	144.7	
1965	150.1	
1966	76.7	
1967	50.9	
1968	62.9	
1969	81.8	
1970	86.8	
1971	90.4	
1972	107.7	
1973	102.9	
1974	34.8	
1975	38.6	
1976	38.5	
1977	44.6	
1978	57.2	
1979	39.5	
1980	35.5	
1981		47.6
1982		33.7
1983		11.3
1984		11.8
1985		12.1



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Review

Haemostatic abnormalities in hepatosplenic schistosomiasis mansoni

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Abstract

Hepatosplenic schistosomiasis is a complex immuno-regulatory disease and is major health problem in endemic countries. Acute bleeding is one of its most serious complications and often life-threatening. Clinical studies have demonstrated that the patients with hepatosplenic schistosomiasis are prone to develop complex haemostatic abnormalities that may be linked to the potential risk of bleeding from ruptured esophageal varices in these patients. The deficit in haemostatic parameters is more pronounced with the advancement of the disease and is maximal in the patients with experience of haematomesis. Evidences of enhanced generation of thrombin and plasmin indicate the presence of low-grade DIC in advanced hepatosplenic schistosomiasis, which is considered as a principal cause of haemostatic abnormalities in this endemic disease. Demonstration of procoagulant expression in peripheral blood monocytes of the patients and in the livers, spleens and intestines of *S. mansoni*-infected mice suggest their possible implication in the causation of DIC in *S. mansoni* infections. Moreover, because in vitro analysis indicates a participation of immune mechanisms in the localized procoagulant expression, it seems likely that the immune responses to schstosomes play a major role in the pathogenic mechanisms of haemostatic abnormalities in hepatosplenic schistosomiasis.

Keywords: Schistosomiasis; *Schistosoma mansoni*; Haemostatic abnormalities; Disseminated intravascular coagulation (DIC); Macrophage; Procoagulant

Abbreviations: AT III, antithrombin III; DIC, disseminated intravascular coagulation; F1+2, prothrombin fragment 1+2; FVIIa, activated factor VII; FXa, activated factor X; FX activator, factor X activator; FDP, Fibrin(ogen) degradation products; FPA, fibrinopeptide A; GM-CSF, granulocyte-macrophage colony-stimulating factor; IFNγ, interferon gamma; IL-1α, interleukin-1alpha; IL-1β, interleukin-1beta; IL-4, interleukin-4; IL-6, interleukin-6; IL-12, interleukin-12; LPS, bacterial lipopolysaccharide; MHV-3, murine hepatitis virus strain 3; NK cell, natural killer cell; PAI-1, plasminogen activator inhibitor-1; PMA, phorbol myristate acetate; SLE, systemic lupus erythematosus; SWAP, soluble worm antigen preparation; TAT, thrombin-antithrombin III complex; TF, tissue factor; TNF α, tumor necrosis factor alpha.

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1. Introduction

Schistosomiasis is endemic in more than 75 countries in Africa, Asia and South America and is a serious health problem in these countries [1]. Bleeding is a common complication and a leading cause of death in patients with schistosomiasis mansoni [2]. Although primary cause of acute attack of haematomesis is considered to be rupture of esophageal varices by portal hypertension, impaired haemostatic and fibrinolytic mechanisms probably exacerbate the haemorrhagic diathesis in the patients with hepatosplenic schistosomiasis. Haematostatic defects are commonly found in this endemic disease and are complex and multifactorial; impaired coagulation [2–9,15,16,26,28], diminished levels of coagulation and anticoagulation factors [3–9], increased thrombin generation [6,8,10,11], and enhanced fibrinolysis [6,8,11] have been observed in the patients with hepatosplenic schistosomiasis. Coexistence of elevated thrombin and plasmin generation [6,8] definitively suggests the presence of steady state of low-grade DIC with and without overt bleeding in hepatosplenic schistosomiasis [6,8]. In this review, we would like to focus on the haemostatic abnormalities in hepatosplenic schistosomiasis and discuss the pathogenic mechanisms implicated in the development of coagulopathy in hepatosplenic schistosomiasis.

2. Haemostatic abnormalities in schistosomiasis mansoni

Clinical studies have demonstrated that the patients with hepatosplenic schistosomiasis develop complex and multifarious haemostatic abnormalities. The marked prolongation of prothrombin time, partial thromboplastin time and thrombin time as well as thrombocytopenia and hypofibrinogenemia [2–9,15,16,26,28] have been found in the patients with compensated and decompensated schistosomiasis mansoni. Defects of vitamin-K-dependent and contact-dependent coagulation have been also demonstrated in these patients; significantly reduced activities of factors II, VII, IX and X [4–6], and significantly lower levels of factors XII and XI, high-molecular-weight kininogen and prekallikrein [3,6] have been found as compared with controls. Investigation of the anticoagulant potential has shown a progressive decrease in the levels of AT III, protein C and protein S in parallel with progress of the disease [6–9]. High FDP level together with the striking rise in F1+2 and TAT levels, and the associated elevation of D-dimer and FPA levels have been observed in both cases with compensated and decompensated hepatosplenic schistosomiasis [6]. The highest level of these factors has been demonstrated in the acute cases with haematomesis from ruptured esophageal varices. This reflects the increased rate of activation of coagulation and fibrinolysis with excessive thromin and plasmin generation in these patients. Other authors also have reported similar results [8,10,11]. A state of low-grade chronic DIC has been reported in clinically stable chronic liver diseases [12–14], in which definitive diagnosis of DIC are conducted by the evaluation of thrombin and plasmin generation. It is, therefore, likely that haemostatic abnormalities found in this endemic disease primarily result from the presence of steady state of low-grade DIC with and without overt bleeding. However, because considerable impairment of liver functions [3,8,9] has been observed in the patients with advanced hepatosplenic schistosomiasis, it is difficult to attribute these haemostatic abnormalities to DIC alone. Moreover, decreased levels of coagulation proteins correlated significantly with the degree of disturbed liver functions [3,8,9]. Accordingly, reduced hepatic synthesis of most haemostatic proteins as well as decreased clearance of activated forms coupled with consumption should be also considered to be responsible for the haemostatic abnormalities in advanced hepatosplenic schistosomiasis.

Hyperfibrinolytic state has been demonstrated in the patients with hepatosplenic schistosomiasis. The progressive increase in F1+2 and D-dimer from compensated to decompensated form [6,8,11] suggests a relationship between the severity of hepatosplenic schistosomiasis and the amount of haemostatic activation. A progressive increase in the levels of plasminogen activator, tissue plasminogen activator, urokinase plasminogen activator, α2-antiplasmin-plasmin complex, FDP and D-dimer in advancement of the disease [10,15] is

consistent with a hyperfibrinolytic state. In addition, there has been a progressive decrease of plasminogen, α2-antiplasmin and PAI-1 levels in decompensated hepatosplenomegaly [15]. Moreover, because PAI-1 has decreased significantly in all diseased groups [11,15,16], accelerated fibrinolysis in schistosomiasis may be due to the progressive increase of plasminogen activator. Similar findings have been already found in chronic liver diseases [17–19], in which increased level of plasminogen activator is thought to be due to decreased clearance by the diseased liver, increased production due to endotoxaemia and excessive thrombin generation followed by hyperfibrinolysis. It is, therefore, possible that disturbed liver function, endotoxaemia and excessive thrombin generation, all of which has been found in the patients with hepatosplenic schistosomiasis [3,6,8–11,26], are responsible for the increase of plasminogen activator and for the hyperfibrinolysis in hepatosplenic schistosomiasis.

What induced the acute attack of bleeding remains unknown. No particular coagulation profile for predictive of haematomesis has been still identified, although many have been suggested [20–22]. However, since hypocoagulable and hyperfibrinolytic state is considered to be potent risk factor of bleeding, it is likely that these defects of haemostatic mechanisms may contribute to the serious haemorrhagic diathesis in hepatosplenic schistosomiasis.

3. Procoagulants in schistosomiasis mansoni

As described above, the patients with hepatosplenic schistosomiasis show a steady state of low-grade DIC with multifarious haemostatic abnormalities, but the mechanism responsible for the development of DIC remains unknown. High levels of F1+2 and TAT in the patients with compensated and decompensated hepatosplenic schistosomiasis [6–8,10,11] indicate the persistent activation of coagulation system and thrombin generation throughout the course of advanced stage. This may be supported by the observation that extensive fibrin deposition has been found over hepatic egg granulomas in *S. mansoni*-infected mice [23], because fibrin deposition is considered as direct evidence indicating the activation of coagulation system and the generation of thrombin [24]. Accordingly, identification of the activating mechanism of coagulation seems to be important for clarification of the pathogenesis in schistosome coagulopathy. In mammalian species vascular endothelium, monocytes/macrophages and other types of cells are capable of producing proteins that actively promote the blood clotting, i.e. procoagulant. Three types of procoagulants, i.e. TF, FX activator and prothrombinase, are known to be produced by these cells in response to various stimuli, such as pro-inflammatory cytokines, lymphokines, LPS, PMA, immune complex and infection, as summarized in Table 1. A significantly higher monocyte TF expression has been recently demonstrated by in vitro experiments using peripheral blood monocytes isolated from the patients with compensated and decompensated hepatosplenic schistosomiasis, as compared with controls [25]. The highest level has been seen in the patients with acute attack of variceal bleeding. In addition, a positive correlation has been noted between serum level of F1+2 and monocyte TF antigen or TF activity [25], which suggesting the association of enhanced monocyte TF expression and prothrombotic state in hepatosplenic schistosomiasis. Moreover, a significantly higher TF expression without LPS stimulation by the monocytes from these patients [25] suggests that monocytes are already activated in vivo. Accordingly, it appears to be important that high levels of LPS, TNFα, IL-1α [26], adhesion molecules [27], platelet factor 4 [11], monocyte chemoattractant protein 1 [28] and immune complexes [6] have been reported in hepatosplenic schistosomiasis, because all of these substances are known to be potent inducers of TF procoagulant by monocytes/macrophages [29–32]. Enhanced monocyte TF expression has been already demonstrated in patients with liver cirrhosis [33,34] and SLE [35], and is considered to be closely associated with the development of coagulopathy in these diseases. It is, therefore, likely that the increased monocyte TF expression may be linked to the coagulopathy in schistosomiasis.

Table 1
Classification of procoagulants in human and laboratory animals

Cells	Species/Cell source	Stimulus	Procoagulants	Reference
Endothelial cells	Human/Umbilical cord	LPS, IL-1α, TNFα	TF	[51–53]
	Human/Umbilical cord	CD40L	TF	[54]
	Human/Umbilical cord	Lymphocytes, PMA	TF	[53,55]
Astrocytes	Mouse/Brain	IL-6, IL-1β, TNFα	TF	[56]
Kupffer cells	Rabbit/Liver	LPS	FX activator	[57]
Macrophages	Bovine/Lung(BAL)	LPS	TF	[58]
	Rabbit/Lung(BAL)	LPS	TF	[59]
	Rabbit/Thymus	LPS	TF	[60]
	Rabbit/Spleen	LPS	TF	[60]
	Rabbit/Bone marrow	LPS	TF	[60]
	Mouse/Peritoneal exudates	MHV-3	Prothrombinase	[61]
	Mouse/Peritoneal exudates	IFNγ	FX activator	[62]
	Mouse/Peritoneal exudates	LPS	FX activator	[63]
Monocytes	Mouse/Blood	LPS	Prothrombinase	[65]
	Human/Blood	TH 1 cells	TF	[66]
	Human/Blood	LPS	TF	[64,67]
	Human/Blood	P-selectin	TF	[68]
	Human/Blood	IFNγ, IL-1β, TNFα	TF	[30]
Fibroblasts	Human/Umbilical cord	Not stimulated	TF	[43]
Vascular smooth muscle cells	Human/Umbilical cord	Not stimulated	TF	[43]

Tanabe and his colleagues have reported the localization of large quantity of procoagulants capable activating FX directly in the livers, spleens and intestines of *S. mansoni*-infected mice (Tanabe M, submitted). From biochemical characterization of the procoagulants purified independently from these three tissues, they are identified as a high molecular weight and high-density lipoprotein with almost same chemical and physical properties. In addition, they had the properties of serine protease and required calcium ions to activate FX. Moreover, disappearance of the activities of these procoagulants by treatment of mice with warfarin suggests that a complex of TF and FVIIa may be responsible for their FX activating activities. Intravenous administration of these procoagulants has caused an acute thrombosis in injected animals; multiple thrombi have been demonstrated in the hearts and lungs of injected animals. In these animals, various haemostatic abnormalities have been also demonstrated, i.e. impaired coagulation, thrombocytopenia, hypofibrinogenemia, and elevation of serum levels of TAT, FDP and D-dimer, as already found in the patients with advanced hepatosplenic schistosomiasis [2–9,15,16,26,28]. In addition, pre-administration of animals with anticoagulants such as heparin, warfarin or nafamostat mesilate could protect effectively these animals from the lethal effects of procoagulants. These findings suggest a possible involvement of localized expression of FX activating procoagulants in the activation of coagulation cascade in the livers, spleens and intestines of *S. mansoni*-infected mice, and also suggest a possibility that localized expression of active procoagulants may be responsible for the impaired coagulation, fibrin deposition in egg granulomas and bleeding from large intestine, all of which have been commonly found in *S. mansoni*-infected mice [23,36]. Although the expression of procoagulants has not been identified in any tissues of the patients, it may be possible that the same pathological mechanism as found in experimental mouse model plays a role in the pathogenesis of DIC in the patients with advanced hepatosplenic schistosomiasis.