STUDIES ON "KASEN" OF HORSES IN HOKKAIDO

V. PRELIMINARY EXPERIMENTS CONCERNING THE EFFECTS OF ANTIALLERGIC DRUGS APPLIED TO HORSES AFFECTED WITH THE DISEASE

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INTRODUCTION

So-called "kasen" of horses in our country has been studied from many years ago, but its real cause and effective therapeutic treatments have not yet been clarified. From 1953, the authors have conducted etiological and therapeutical studies[6~11] on "kasen" of horses in Hokkaido.

On the basis of results obtained from their investigations, they have reached an opinion that the disease may be related to a certain allergic reaction because of the similarity of this disease to Queensland itch or allergic dermatitis reported by RIEK[14,15]. Especially, as was described in the research on the actual state[9], the authors have come to suspect that the disease may be caused by the development of a hypersensitivity to the bites of some insects. Based upon such considerations, experimental treatments for 32 affected animals were tried by the injections of antihistamine preparations and the spray of insecticides in the summers of 1955 and 1956. Investigation of the relationship between the disease and allergic reaction was undertaken. In the course of the experiments, clinical and hematological studies were made. Taking a general view of the experiments, disappearance of the itchiness and reduction of the severity of lesions were observed respectively as results of the treatments. Then blood histamine quantitative and eosinophile numbers ran in parallel with the disappearance of the itchiness and decrease of the severity of the lesions. Therefore, from the results of the therapeutic experiments, the authors obtained a few significant items of knowledge which are considered to be most important information relative to research on the disease. In this paper, the influence that antihistamine therapy exerted over "kasen" and the variations of the blood constituents in the course of the experiment are described.

EXPERIMENTAL MATERIALS AND METHODS

General view of the experimental methods is shown in table 1.

Experimental horses and drugs Thirty-two affected horses were used for the experiment; they were well nourished, 2 to 15 years old, black or black-brown in hair color, male or female mongrel Percherons. They were engaged in farm work almost every day. Fourteen cases out of them were carried out in 1955 and the other 18 cases in 1956. The horses had all been attacked by the disease in every summer over a period of from 2 to 13 years. Besides this, 7 non-affected horses were used as control for the experiments of comparing the clinical syndromes and the constituents of blood with those of the patients.

Therapeutic drugs applied Allergin (Chlorprophenpyridamine maleate)*, Venacalcium B_6 (Diphenhydrochloride, Bromcalcium and Vitamine B_6)** and Hiberna (Promethazine hydrochloride)***; they are all antihistamine preparations.

The affected horses, as indicated in table 1, were divided into 5 groups in accordance with the kind of drugs administered.

Therapeutic methods The 1st group consisted of 14 cases. Allergin was injected subcutaneously at the amount of 200 mg per day for 5 days. The animals were treated at periods of most serious conditions from July to August, 1955, viz., 5 cases were in the middle of July, 5 cases were in the late part of July and the other 4 cases were in the late part of August, respectively. The 2nd group consisted of 5 cases which showed already serious syndromes of "kasen". Allergin was injected subcutaneously at the rate of 300 mg per day for 5 days in the middle part of July. In the 3rd group, 3 serious cases were treated by intravenous injection of Venacalcium B_6 in the amount of 200 mg per day for 5 days in late June. In the 4th group, Hiberna was injected intravenously at the rate of 200 mg per day for 5 days in the late part of August for 5 serious cases. In the 5th group, which also consisted of 5 cases, Allergin was injected subcutaneously at the amount of 100 mg per day for 5 days, for the purpose of preventing the onset, in the middle of June.

Extermination of the bloodsucking insects DDT (5~10%) and BHC (1.5~3%) powders were used in parallel with the injections of the antihistamine preparations. Insecticides were mainly sprayed over the areas of long hair in the neck and tail and in the vicinity of the stables by the owners for the purpose of exterminating the bloodsucking insects or preventing the bites of the insects. However, in disregard of instructions, this work was not practiced except for a few cases. In only one case of the 4th group, use was made of Fumakiller which was manufactured for the extermination of insects as an oil preparation of pyrethrum. The biting insects had grown numerous about at the middle of June. In the 5th group, insecticides were not used intentionally from the commencement of the injections for the purpose of observing the etiological significance of the bites of the bloodsucking insects.

* Manufactured by Sankyo Co., Ltd., Tokyo.
** Manufactured by Tanabe Pharmac. Co., Ltd., Osaka.
*** Manufactured by Yoshitomi Pharmac. Co., Ltd., Osaka.

TABLE 1. *Therapeutic Methods*

GROUP	CASE NOS.	MEDICINE	DOSIS	METHOD OF INJECTION	TIME OF INJECTION
I	14 (No. 1~14)	Allergin	*200 mg/day for 5 days	Subcutaneously	from July to August in 1955
II	5 (No. 15~19)	"	*300 mg/day for 5 days	"	July in 1956
III	3 (No. 20~22)	Venacalcium B_6	**200 mg/day for 5 days	Intravenously	"
IV	5 (No. 23~27)	Hiberna	***200 mg/day for 5 days	"	August in 1956
V	****5 (No. 28~32)	Allergin	*100 mg/day for 5 days	Subcutaneously	June in 1956

* Real volume of chlorprophenpyridamine maleate.
** Real volume of diphenhydrochloride.
*** Real volume of promethazine hydrochloride.
**** Carried out for prevention.

Blood examination In the course of the experiments, blood cell numbers, differential counts of leucocytes, total serum protein and its fractions, blood sugar levels, serum inorganic phosphorus and calcium, and the concentrations of blood plasma histamine were measured, respectively. The biochemical analysis of blood constituents was conducted by photoelectric photometer and histamine concentrations were estimated by KOMAKI's[3] which was modified from LUMBSCHEZ's method.[5]

Examinations of variations in the blood constituents for the year For the sake of comparison of the blood constituents of the affected and non-affected horses throughout the year, 10 affected and 4 normal horses were used. Patients were well nourished, female mongrel Percherons which suffered every year from the disease. Normal horses were also well nourished, mongrel Percherons and quite free from "kasen" and other disease. The blood examinations were conducted in the late part of May, late in August, late in November and in the late part of February respectively. The methods of the examinations were same as they were made in the treatment groups.

RESULTS OF INVESTIGATIONS

Clinically, inspections and palpations were performed on all cases through the experiments. General data on the alterations of severity of the disease as influenced by the treatments are shown in table 2.

The 1st group Injections of Allergin and spraying of BHC and DDT were conducted. From the 2nd and 3rd days of the injections remarkable decrease of itchiness was found in all cases. At the end of the treatment, disappearance of the itchiness was found in all patients and they seemed to become to be quite well, but 4 cases out of them

TABLE 2. *Alterations in the Severity of the Disease Influenced by Treatments*

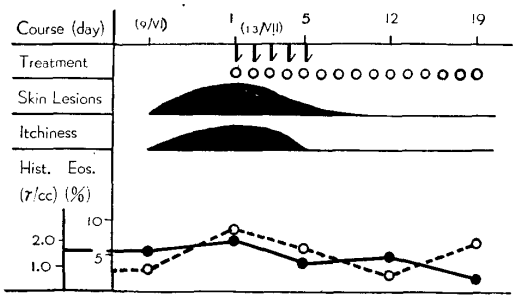
GROUP	APPLIED MEDICINE	CASE NOS.	SEVERITY OF THE DISEASE					SPRAY OF INSECTICIDE
			Just before Injection	Just after Injection	1 Week after Injection	2 Weeks after Injection	4 Weeks after Injection	
I	Allergin	1	+	−	−	−	.	○ D
		2	++	±	−	−	.	○ "
		3	++	±	±	+	.	◓ "
		4	++	+	+	+	.	● "
		5	++	+	±	+	.	● "
		6	+	±	±	−	.	● B
		7	+	±	−	+	.	○ "
		8	++	−	−	±	.	○ "
		9	++	+	+	++	.	○ "
		10	++	++	++	++	.	● "
		11	++	±	−	−	.	○ "
		12	++	++	++	++	.	● "
		13	++	+	±	±	.	◓ "
		14	++	−	±	−	.	○ "
II	Allergin	15	++	±	+	.	.	●
		16	++	−	++	.	.	●
		17	+	−	±	.	.	●
		18	++	−	++	.	.	●
		19	+	−	±	.	.	●
III	Venacalcium B_6	20	++	−	−	.	−	◎ B
		21	+	−	+	.	+	◓ "
		22	++	±	+	.	++	● "
IV	Hiberna	23	++	±	−	.	.	◎ D
		24	++	±	−	.	.	○ "
		25	++	+	+	.	.	◓ "
		26	++	±	+	.	.	◓ "
		27	++	−	−	.	.	○ F
V	Allergin	28	−	−	±	.	.	●
		29	−	−	+	.	.	●
		30	−	−	+	.	.	●
		31	−	−	±	.	.	●
		32	−	−	+	.	.	●

◎ ····· Insecticide was sprayed sufficient.
○ ◓ ····· Insecticide was sprayed insufficient.
● ····· Insecticide was not sprayed

B ····· BHC
D ····· DDT
F ····· Fumakiller

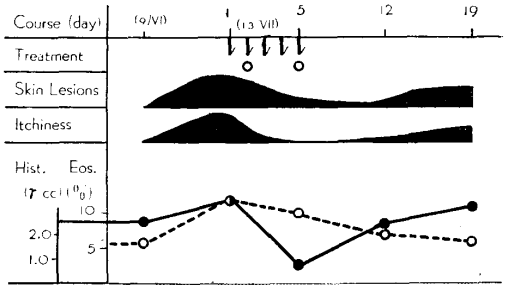
showed relapse at one week after the injections. Moreover, 3 other cases relapsed 3 weeks later. In the recovered 7 cases, the use of the insecticides was sufficient and they were further continued every day even after the injections were discarded. However, in the relapsed animals, the spray of the insecticides was insufficient or had almost no effects. In the skin lesions of the recovered cases, softening of the skin, desiccation and scurf or crust formations were found. In a few cases, although depression was observed owing to the injections, no other clinical changes were found. The absorption of the medicine injected subcutaneously was so slow that the edematous swelling remained until about 2 days after. Two treated cases are shown in charts 1 and 2.

CHART 1. *Course of Treatments in Recovered Case No. 2*
(Allergin 200 mg/day)



○ ··· Spray of DDT
↓ ··· Injection

CHART 2. *Course of Treatments in Relapsed Case No. 5*
(Allergin 200 mg/day)

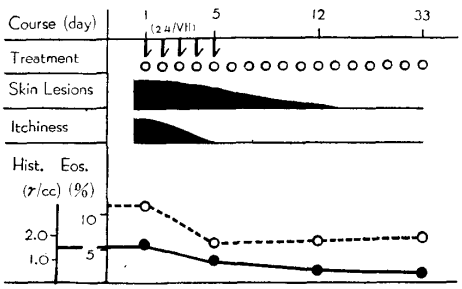


○ ··· Spray of DDT
↓ ··· Injection

The 2nd group In the 2nd group, Allergin was injected intravenously and no spray of insecticide was conducted throughout the experiment. Although, in view of the clinical findings, the itchiness in all cases seemed to disappear just after the injections, they all relapsed again at one week after the conclusion of injections. The relapses seemed to have no connection with use of the insecticides.

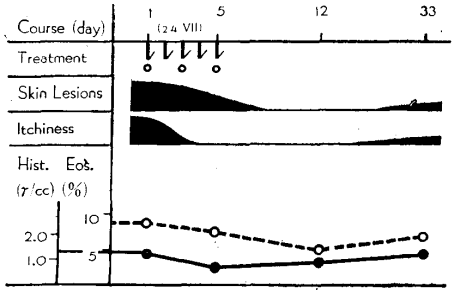
The 3rd group Venacalcium B_6 was injected intravenously and BHC was sprayed sufficiently in this group, and beneficial results were obtained. But 2 cases where the use

CHART 3. *Course of Treatments in Recovered Case No. 20*
(Venacalcium B_6 200 mg/day)



○ ··· Spray of BHC
↓ ··· Injection

CHART 4. *Course of Treatments in Relapsed Case No. 22*
(Venacalcium B_6 200 mg/day)

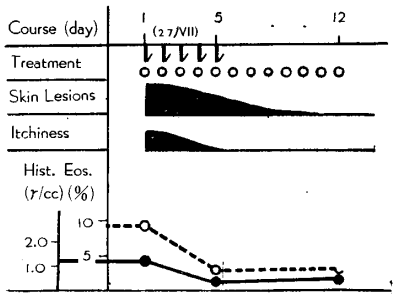


○ ··· Spray of BHC
↓ ··· Injection

of the insecticide was neglected from after the injections showed reappearances of itchiness in the lesions about 1 week later. In 1 out of 3 cases, complete recovery was found because of the extermination of insects was practised exactly from before injections and also continued for a long period after the injections. Two treated cases are shown in charts 3 and 4.

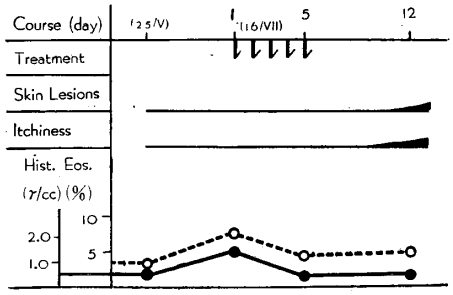
The 4th group Five patients were treated with Hiberna intravenously and DDT was sprayed. Three cases recovered quite well, but in 2 cases no beneficial effects were obtained. In the latter cases, it is thought that the spraying of DDT was not done carefully and the relapses were found at one week after injections. One treated case is shown in chart 5.

CHART 5. *Course of Treatments in Recovered Case No. 23*
(Hiberna 200 mg/day)



○ ··· Spray of DDT
↓ ··· Injection

CHART 6. *Prophylactic Use of Allergin in Case No. 31*
(Allergin 100 mg/day)



↓ ··· Injection

The 5th group The horses were not yet affected at the commencement of the injections. This group was treated with Allergin and with non-spray of insecticide for the purpose of preventing the onset of itchiness, however the appearance of itchiness in the long-hair regions was observed about 1 or 2 weeks after the injections. The experiment was conducted in the middle of June and seemingly the bloodsucking insects appeared from the end of the injections. Consequently, the present preventive experiment resulted in complete failure. One treated case is shown in chart 6.

HEMATOLOGICAL FINDINGS

Relations among the Histamine Contents, Eosinophile Counts and the Itchiness

Characteristic alterations in the blood examinations of the affected group were found in the blood histamine concentrations and in the eosinophile counts. Alterations were decreased gradually by the injections of antihistamine preparations. In the blood findings, no remarkable differences were observed between the affected and non-affected groups except mainly in the blood histamine concentration and in the eosinophile counts. The histamine contents and the eosiniphile counts in the non-affected group showed comparatively constant values throughout the experiments. On the other hand, both of the values in the affected animals were higher than those of non-affected animals. These variations

TABLE 3. *Mean Values of the Blood Findings*

GROUP	BLOOD CONSTITUENTS	ONSET OF ITCHINESS	JUST BEFORE INJECTION	JUST AFTER INJECTION	1 WEEK AFTER INJECTION	2 WEEKS AFTER INJECTION	4 WEEKS AFTER INJECTION
Therapeutic Group (27)	R. (mill.)	673.00	675.00	585.00	665.00	678.00	588.00
	W.	8140.00	9123.00	8572.00	8946.00	8350.00	9332.00
	Eos. (%)	4.20	6.90	4.00	4.10	4.50	7.20
	T.P. (g/dl)	6.70	6.90	6.90	7.10	7.30	6.90
	Alb. "	2.00	2.33	2.17	2.30	3.60	2.60
	Grob. "	4.80	4.60	4.75	4.73	3.70	4.43
	α- "	.	0.85	1.32	0.99	1.06	0.42
	β- "	.	2.29	2.32	2.22	0.65	1.15
	γ- "	.	1.38	1.29	1.44	2.10	2.90
	A/G	0.44	0.52	0.48	0.52	0.96	0.58
	Sugar (mg/dl)	67.00	92.50	73.00	76.80	82.00	79.00
	P "	3.80	4.50	6.90	4.70	4.50	11.90
	Ca "	11.90	9.70	9.60	10.60	12.60	13.40
	Hist. (γ/ml)	1.40	1.80	0.93	1.11	1.80	0.90
Prophylactic Group (5)	R. (mill.)	657.00	755.00	763.00	999.00		
	W.	9120.00	1168.00	9570.00	11680.00		
	Eos. (%)	2.00	5.30	5.50	3.30		
	T.P. (g/dl)	6.40	6.80	7.00	6.70		
	Alb. "	2.74	2.10	2.35	2.15		
	Grob. "	3.66	4.70	4.65	4.54		
	α- "	0.31	1.08	0.64	1.18		
	β- "	0.75	0.99	1.36	0.78		
	γ- "	2.70	2.40	2.40	2.56		
	A/G	0.67	0.45	0.50	0.47		
	Sugar (mg/dl)	97.00	116.40	99.30	101.00		
	P "	3.50	5.20	3.30	3.50		
	Ca "	12.10	11.30	11.40	10.60		
	Hist. (γ/ml)	1.16	2.05	0.44	0.88		
Non-treated Normal Group (7)	R. (mill.)	685.00	675.00	677.00	700.00		
	W.	8270.00	8620.00	7952.00	8172.00		
	Eos. (%)	1.30	4.10	3.30	3.20		
	T.P. (g/dl)	6.30	6.60	6.50	7.00		
	Alb. "	2.30	2.60	2.10	1.60		
	Grob. "	4.00	4.00	4.40	5.40		
	α- "	.	0.55	1.00	0.75		
	β- "	.	2.20	1.30	2.45		
	γ- "	.	1.30	2.10	2.65		
	A/G	0.58	0.65	0.48	0.30		
	Sugar (mg/dl)	65.50	96.00	54.00	54.00		
	P "	5.60	3.30	3.90	4.70		
	Ca "	12.30	12.80	11.60	11.50		
	Hist. (γ/ml)	1.25	1.15	0.80	1.25		

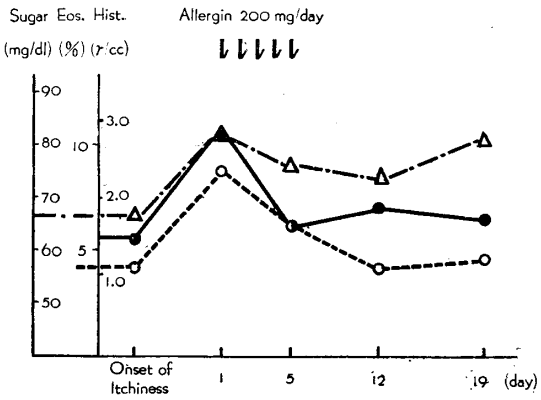
almost kept pace with variations of the clinical syndromes and also, though it was not remarkable, with that of the blood sugar levels. Particularly, the relations among the histamine contents, eosinophile counts and the itchiness were of most important sig-

nificance. The respective average value of the blood findings in the therapeutic group, the prophylactic group and in the non-affected group are indicated in table 3. Red and white cell numbers, the values of serum protein, inorganic phosphorus and of calcium indicated no conspicuous variations.

Relations between the Eosinophile Counts and the Histamine Contents

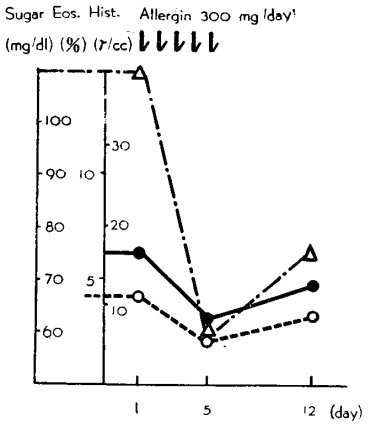
The 1st group At the onset of the itchiness in the early part of June, the average values of the eosinophile counts and the histamine contents in 14 affected animals were 4.2 (2.0~9.0)% and 1.40 (0.72~3.80) γ/ml. At just before injections in the severest periods of the conditions, they increased to 10 (2.0~15.0) % and 2.90 (2.00~3.90) γ/ml respectively. When the Allergin was injected for 5 days all cases upon the clinical inspections were recognized to recover, and the histamine and eosinophile values decreased to 5.4 (2.0~15.0) % and 1.70 (0.60~2.65) γ/ml respectively. At the end of the observations at one week after injections, they indicated 4.1 (1.0~10.0) % and 1.90 (1.20~2.55) γ/ml. At 4 weeks after the injections, they showed 4.0 (1.5~11.5) % in the eosinophile counts and 1.65 (0.70~3.70) γ/ml in the histamine contents. The variations of mean values in the 1st group are shown in chart 7.

CHART 7. *Variations of Mean Values of Histamine Contents, Eosinophile Counts and Blood Sugar in Group I*



↓ ··· Injection

CHART 8. *Variations of Mean Values of Histamine Contents, Eosinophile Counts and Blood Sugar in Group II*



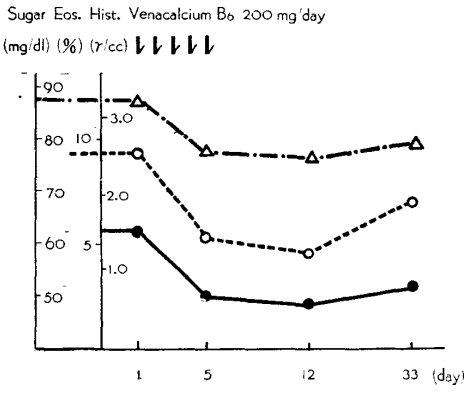
↓ ··· Injection

The 2nd Group The mean values of the eosinophile counts in 5 cases were 9.2 (6.5~13.0) % at just before injections, 1.9 (0.5~2.5) % at just after injections and 2.3 (1.5~7.5) % at 1 week after injections; the histamine contents were 1.78 (1.46~2.00) γ/ml, 0.8 (0.50~1.34) γ/ml and 1.32 (0.34~2.14) γ/ml respectively. Both the values were decreased by the injections, but in the observations at 1 week after injections, a tendency toward increase was found in accordance with the relapses. The variations of mean values in the 2nd group are indicated in chart 8.

The 3rd group Three affected animals were injected with Venacalcium B_{12} and the insecticides was BHC. The eosinophile counts were 9.2 (6.5~13.0) % at just before injections, 5.3 (2.7~7.5) % at just after injections and 4.7 (3.0~7.0) % at 1 week after injections; the histamine contents were 1.74 (1.22~1.86) γ/ml, 0.64 (0.50~0.82) γ/ml and 0.55

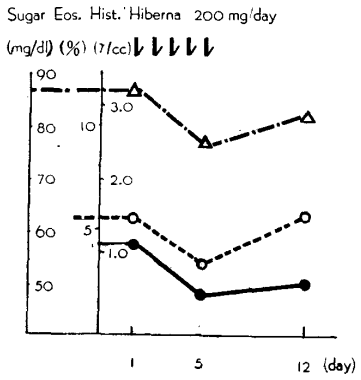
(0.24~0.68) γ/ml respectively. Namely decrease of these values was found as resultant from the injections, however, they increased to 7.2 (4.0~13.0) % and 0.60 (0.42~0.82) γ/ml respectively at 4 weeks after injections. This was due to the relapses in 2 cases. The variations of mean values in the 3rd group are shown in chart 9.

CHART 9. *Variations of Mean Values of Histamine Contents, Eosinophile Counts and Blood Sugar in Group III*



↓ ··· Injection

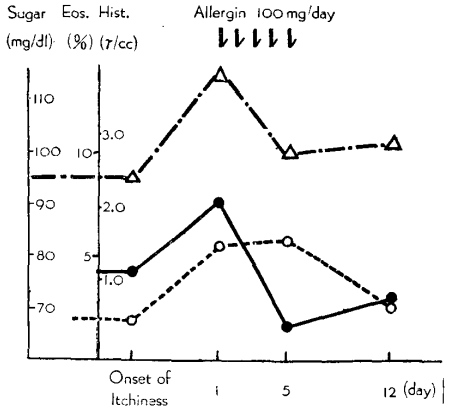
CHART 10. *Variations of Mean Values of Histamine Contents, Eosinophile Counts and Blood Sugar in Group IV*



↓ ··· Injection

The 4th group Five affected horses were injected with Hiberna and DDT was used. The eosinophile counts at just before injections, at just after injections and about one week after injections were 5.6 (2.0~8.5) %, 3.3 (1.5~6.5) % and 5.2 (1.5~10.0) % respectively. The histamine contents were 1.70 (0.95~1.95) γ/ml, 0.53 (0.42~0.68) γ/ml and 0.67 (0.42~1.00) γ/ml. They ran almost parallel with the alterations of clinical syndromes as was found in other treated groups. The variations of mean values of the 4th group are shown in chart 10.

CHART 11. *Variations of Mean Values of Histamine Contents, Eosinophile Counts and Blood Sugar in Group V*



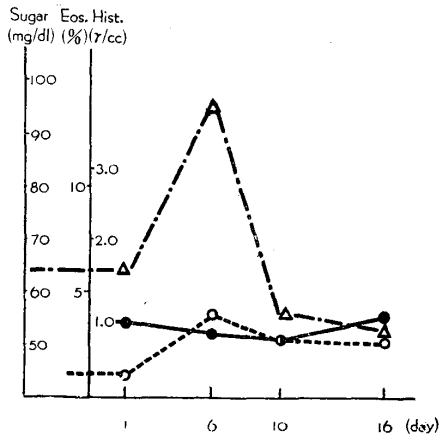
↓ ··· Injection

The 5th group Five cases were injected with Allergin for 5 days before attacks. No insecticide was used. The eosinophiles were counted as 5.3 (3.0~7.5) % and the histamine concentrations were measured as 2.05 (1.35~2.53) γ/ml at before injections. When the injections ended the eosinophile count was 5.5 (2.0~10.5) % and the histamine content was 0.43 (0.40~0.50) γ/ml. On the examinations of 1 week after the injections, they were 3.3 (1.0~6.0) % and 1.32 (0.34~2.14) γ/ml respectively and the itchiness was found in all cases in the neck and in the tails. So, the animals were thought to be attacked despite the injections because the insecticides were not sprayed. The variations of mean values of the 5th group are

indicated in chart 11.

The non-treated normal group The blood of 7 non-affected horses were offered to the blood examination. The times for the blood examination were in the late of July, 1956; they were corresponded to that of the 5 cases in the 2nd group. The blood examination was conducted 4 times at intervals of 5~7 days with no injections in parallel with the treated group. The mean values of eosinophile counts were 1.3%, 4.1%, 3.3% and 3.2%, and the histamine contents were 1.25 γ/ml, 1.15 γ/ml, 0.80 γ/ml and 1.25 γ/ml respectively. The variations of mean values were shown in chart 12.

CHART 12. *Variations of Mean Values of Histamine Contents, Eosinophile Counts and Blood Sugar in Non-treated Group*



The Variations in the Blood Constituents for the Year

Ten affected and 4 non-affected horses were used for the examination. The blood samples were examined in May (29, 30/V '55), August (17, 20/VIII '55), November (20, 21/XI '55) and February (13, 14/II '56). The results are shown in table 4 and chart 13. In both groups, the blood cell numbers, serum protein, serum inorganic phosphorus and serum calcium showed no obvious variations throughout the year. However, alterations in the blood histamines and eosinophile counts were noticeable.

In the affected group, the average values of the histamine contents were measured as 1.96 γ/ml, 2.99 γ/ml, 1.70 γ/ml and 0.84 γ/ml and that of the eosinophile numbers were counted as 4.2%, 9.1%, 4.4% and 3.4% respectively. In the non-affected group, the average values of the former were 0.58 γ/ml, 0.82 γ/ml, 0.96 γ/ml and 0.48 γ/ml, and that of the latter were 2.3%, 4.1%, 3.5% and 2.8%. On the other hand, the blood sugar levels were 67.1 mg/dl, 80.2 mg/dl, 84.2 mg/dl and 80.4 mg/dl in the affected group, while in the non-affected group, 61.0 mg/dl, 87.5 mg/dl, 71.0 mg/dl and 81.5 mg/dl were measured respectively. From the above data it may be said that the blood histamine and the eosinophiles have the highest value in the summer and have lowest value in the winter. The variations of the 2 constituents in the affected group were parallel with the variations of the conditions of the disease. Especially in the affected group, the variations were more

CHART 13. *Relations among Histamine Contents, Eosinophile Counts and Itchiness in Affected and Non-affected Animals for the Year*

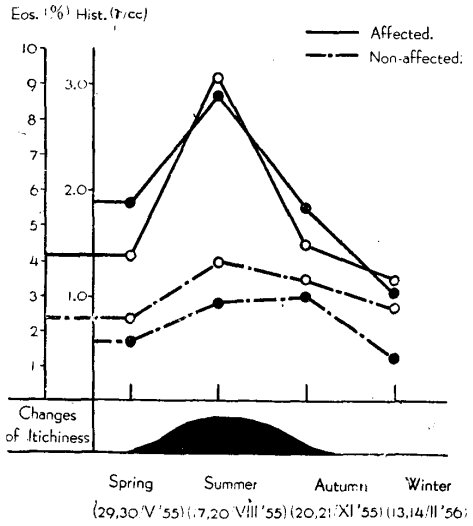


TABLE 4. *Variations in the Blood Constituents for the Year*

GROUP	BLOOD CONSTITUENTS	SPRING	SUMMER	AUTUMN	WINTER
Affected Group (10)	R. (mill.)	673.00	676.00	681.00	655.00
	W.	8200.00	8600.00	8900.00	7800.00
	Eos. (%)	4.20	9.10	4.40	3.40
	T. P. (g/dl)	6.90	7.60	7.20	6.60
	Alb. "	2.00	2.20	3.62	2.70
	Glob. "	4.90	5.50	3.65	3.85
	α- "	1.15	1.00	1.35	1.55
	β- "	2.30	3.00	0.95	1.85
	γ- "	1.35	1.50	1.35	0.45
	A/G	0.44	0.39	0.93	0.70
	Sugar (mg/dl)	67.10	80.20	84.20	80.40
	P "	3.80	4.60	4.70	3.50
	Ca "	11.60	11.00	12.30	11.00
	Hist. (γ/cc)	1.96	2.99	1.70	0.84
Non-affected Group (4)	R. (mill.)	728.00	718.00	839.00	683.00
	W.	9600.00	9200.00	8300.00	7400.00
	Eos. (%)	2.30	4.10	3.50	2.80
	T. P. (g/dl)	6.80	6.80	7.00	6.80
	Alb. "	2.98	2.50	2.84	3.20
	Glob. "	3.83	4.31	4.19	3.57
	α- "	1.20	0.85	1.35	1.20
	β- "	1.65	2.45	1.00	1.25
	γ- "	1.00	1.00	1.85	0.95
	A/G	0.78	0.58	0.68	0.89
	Sugar (mg/dl)	61.00	87.50	71.00	81.50
	P "	3.70	3.40	4.20	4.60
	Ca "	12.20	12.30	11.10	10.40
	Hist. (γ/cc)	0.58	0.82	0.96	0.48

Note: Numbers indicated mean values.

conspicuous than in the non-affected group. The values of the blood sugar levels in the affected group had a tendency of gradual increase toward the winter, but in the non-affected group, no definitive variations were found.

DISCUSSION

The authors have reported their studies on "kasen" of horses in Hokkaido. On the basis of the investigations[6~11] some information useful to research on the cause and therapy has been contributed. Although "kasen" had been believed for a long period to be caused by only microfilaria of *Onchocerca cervicalis*, the authors, ISHIHARA and UENO[1,2] and UENO and ISHIHARA[18,19] have reached the opinion from the experimental results that the so-called "kasen" in Japan is an allergic disease; perhaps it may be caused by the development of a hypersensitivity to the bites of some bloodsucking insects. Queensland itch or allergic dermatitis in

Australia reported by RIEK[14,15] is due to the bites of the sandfly, *Culicoides robertsi*. Comparing the syndromes of "kasen" with those of his descriptions, it has a strong resemblance to Queensland itch, however, the causal agent for the allergic reaction in "kasen" is not yet clarified. On the other hand some investigators are thinking of a microfilarial allergy.

In the present experiments, based upon the previous investigations[6~11], the authors have tried an antiallergic therapy by the injections of antihistamine preparations and by the spray of insecticides. In the injections of antihistamine preparations alone, no effective results were obtained, and even if it seemed to be completely recovered from the itchiness reappeared in several days after the injections. When the insecticides were sprayed sufficiently in parallel with the injections and when they were used continuously for a longer period furthermore, the complete recoveries and no relapses were found. Depending upon the relations among the appearance of the bloodsucking insects, the season, the weather, the atmospheric temperature, the course of the disease and the results of the therapeutic experiments, it may be said with certainty that the disease has a close connection with some bloodsucking insects.

On the blood examinations, characteristic findings were obtained in variations of eosinophile counts and histamine contents. The eosinophile numbers almost ran parallel with the variations of the histamine values, and the variations in both blood constituents paralleled the variations in the conditions of the disease, i. e., they indicated remarkable increase in the serious stage but decreased gradually as a results of the treatments. There was no question that the itchiness disappeared. With respect to the seasonal observations for the year in the both blood constituents, they indicated the highest values in the summer and the lowest in the winter. These variations were identical with those of the severity of the disease.

RIEK reported that in non-affected horses histamine contents and eosinophile counts were comparatively constant throughout the day and the year. Whereas in susceptible horses, they fluctuated widely as compared with those of non-susceptible to allergic dermatitis. Histamine is a normal constituent of the blood and the body, and it exists in constant amount in normal animals. Generally, it is believed[4,17,20] that the increase in body histamine contents is found in allergic disease and the development of the alarming conditions for the body is observed. Also, students are thinking it a fact that eosinophile leucocytes are carriers of histamine. Besides this, in the blood findings of the patients, the blood sugar levels revealed an identical tendency with the changes of the 2 constituents. On the relations among histamine, antihistamine preparations and blood sugar levels, fundamental experiments have been made by several inves- tigators[12,13,16].

By consultation of these references, interesting suggestions for further research on "kasen" may be found.

From the above described data, it may be implied that the existence of the close relations among the clinical findings, eosinophile counts, histamine contents and bloodsucking insects have been found. ISHIHARA and UENO[1,2] and UENO and ISHIHARA[18,19] reported about the geographical distributions of insects and immunological studies on "kasen". YAMASHITA et al.[21] collected several species of sandfly infesting the lesions of the patients and also the present authors[9] have pointed out a close connection between the disease and the bloodsucking insects from the results of the research on the actual state of the disease. However, it is yet unknown by just what kinds of insects the patients were attacked.

In the studies on allergic disease, it is necessary to pay attention to hereditary dispositions. ISHIHARA and UENO reported that "kasen" is one of the diseases having the idiosyncracy of being transmitted by a progenitor, i.e., it belongs to atopy. The ages[6~9] of initial attacks, do not provide evidence to support his idea. However, at any rate, considering the results obtained from the present experiments, the decreases or recoveries of syndromes were found to result from the injections with antihistamine preparations, and the complete recovery may be expected to follow the continual satisfactory spray of insecticides.

SUMMARY

In 1955 and 1956 the authors have conducted therapeutic experiments in "kasen" of horses by the injections of antihistamine preparations and the spray of insecticides. The responses by the affected animals to the drugs applied were examined. The results thus obtained may be summarized as follows.

1. Antihistamine preparations, for instance Allergin, Venacalcium B_6 and Hiberna, are effective drugs for the treatments of "kasen". The schedule applied in the present experiments was 200~300 mg (as real volume of the antihistamine substance) per day for 5 days in each drugs. When the patients were treated with antihistamine preparations alone, the recoveries were temporary and no complete healing was expected. Relapses were observed several days after injections.

2. In the cases where the insecticides were used every day in sufficient amount in parallel with the injections of the drugs, beneficial effects were found. Also, when the insecticides were sprayed after the end of the injections, no relapsed cases were found. Therefore, no expectations for the complete recovery may be obtained without extermination of the bloodsucking insects.

3. In the blood examinations, characteristic findings were noted in the

eosinophile counts and in histamine concentrations. The values of both blood constituents in the affected animals were increased over those of the non-affected animals. When the patients were treated with antihistamine preparations the values of the eosinophiles and blood histamine were gradually decreased, and the variations of both constituents ran almost parallel with the variation of the clinical syndromes. In the other blood constituents, no remarkable variations were observed in the affected and non-affected animals throughout the experiments.

4. The seasonal variations of the histamine contents and eosinophile counts were examined for the year. Their values in the affected animals were shown to be highest in sultry season and lowest in cold season, whereas no obvious changs were found in the non-affected animals. The variations were identical with that of the clinical syndromes and also with the appearance and disappearance of the bloodsucking insects.

5. From the above described data, it may be thought that "kasen" is an allergic disease, and it may be considered to be caused by the development of hypersensitivity to the bites of some bloodsucking insects or by some other factor. Therefore, in the treatments for the disease, it may be considered that it is indispensable to use the antihistamine preparations and to use the insecticides. Especially, the continual spray of the insecticides may have important significance.

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