Studies on the Detoxicating Hormone of the Liver (Yakriton).

25th Report.

Therapeutic Experiment with Yakriton* for Subacute
Phosphorus Poisoning.

By

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Therapeutic experiments with yakriton have been made in our pediatric department with excellent results. Reports concerning these will be made in our clinical periodicals. The present paper treats of therapeutic experiments with yakriton for phosphorus poisoned rabbits. We have already reported the prophylactic use of yakriton for phosphorus intoxication. As already reported, we were surprised at the use of such small amounts (small numbers of R. A. U.) of yakriton, which were just optimum for the prevention of acute¹⁾ and subacute²⁾ phosphorus poisoning.

In spite of my knowledge of the prophylactic efficacy of the small numbers of yakriton units, I was far from presuming the beneficial effect of small numbers of units of it for therapeutic purposes, even though I thought that the general rule in medicine—prophylactically a smaller amount, therapeutically a larger amount—could probably not be applied here freely. Here again I was surprised at the beneficial effect of the small amounts of yakriton for therapeutic purposes.

Experiments.

Subacute phosphorus poisoning was produced by peroral administration of watery “Nekoirazu” emulsion, a kind of ratsbane, and yakriton

*) Throughout this experiment insoluble (emulsified) yakriton was used.

1) K. Asakura, Tohoku J. Exp. Med., 1930, 15, 476.

2) K. Asakura and T. Sato, Tohoku J. Exp. Med., 1929, 13, 180.

was injected in one series of experiments, one hour later, in the other, 6 hours later.

The results are shown in Tables.

TABLE I.

Subacute phosphorus poisoning with 0.5% "Nekoirazu" emulsion.

No. of rabbits	Body weight (kilos)	Amount (c.c.) of "Nekoirazu" emulsion (0.5%) per os used (c.c.)	Result of experiment (†=death in)	Mor- tality (%)	Average days of survival
No. 1 (No. 3100)	1.86	18.6	† 2 days	100	(of 10 rabbits) 2.3 days
No. 2 (No. 3101)	1.85	18.5	† 3 "		
No. 3 (No. 3102)	1.65	16.5	† 2 "		
No. 4 (No. 3103)	1.77	17.7	† 3 "		
No. 5 (No. 3104)	1.68	16.8	† 2 "		
No. 6 (No. 3105)	2.53	25.8	† 2 "		
No. 7 (No. 3106)	1.80	18.0	† 2 "		
No. 8 (No. 3107)	1.75	17.5	† 2 "		
No. 9 (No. 3108)	1.75	17.5	† 2 "		
No. 10 (No. 3109)	1.42	14.2	† 3 "		

These experiments in Table I were not done on one and the same occasion, but are a collection of control experiments performed on the same occasions as the proper experiments tabulated in Tables II-III.

TABLE II.

Therapeutic effect of yakriton used after 1 hour in the case of subacute phosphorus poisoning with 0.5% "Nekoirazu" emulsion.

No. of rabbits	Body weight (kilos)	Yakriton, subcutaneously used, 1 hour after the ad- ministration of phosphorus	Amount of "Nekoirazu" emulsion (0.5%) per os used (c.c.)	Result of experiment (†=death in)	Mor- tality (%)	Average days of survival (of those dead animals alone)
No. 1 (No. 3110)	2.19	$\frac{1}{2}$ R.A.U.	21.9	remained in life	50	(of 5 rabbits) 3 days
No. 2 (No. 3111)	2.48		24.8	† 3 days		
No. 3 (No. 3112)	2.10		21.0	† 3 "		
No. 4 (No. 3113)	1.20		12.0	remained in life		
No. 5 (No. 3114)	1.32		13.2	"		
No. 6 (No. 3115)	2.20		22.0	† 5 days		
No. 7 (No. 3116)	1.90		19.0	† 2 "		
No. 8 (No. 3117)	2.25		22.5	remained in life		

No. of rabbits	Body weight (kilos)	Yakriton, subcutaneously used, 1 hour after the ad- ministration of phosphorus	Amount of "Nekoirazu" emulsion (0.5%) per os used (c.c.)	Result of experiment (†=death in)	Mor- tality (%)	Average days of survival (of those dead animals alone)
No. 9 (No. 3118)	1.55		15.5	remained in life		
No. 10 (No. 3119)	1.30		13.0	† 2 days		
No. 11 (No. 3120)	1.70		17.0	remained in life		
No. 12 (No. 3121)	1.62		16.2	† 2 days		
No. 13 (No. 3122)	1.25		12.5	† 3 "		
No. 14 (No. 3123)	1.67		16.7	remained in life		
No. 15 (No. 3124)	2.15	¼ R.A.U.	21.5	† 4 days	60	(of 6 rabbits)
No. 16 (No. 3125)	1.40		14.0	† 2 "		2.8 days
No. 17 (No. 3126)	1.85		18.5	† 3 "		
No. 18 (No. 3127)	1.50		15.0	† 3 "		
No. 19 (No. 3128)	1.60		16.0	remained in life		
No. 20 (No. 3129)	1.56		15.6	"		
No. 21 (No. 3130)	1.72		17.2	† 2 days		
No. 22 (No. 3131)	1.50		15.0	† 2 "		
No. 23 (No. 3132)	1.72		17.2	† 2 "		
No. 24 (No. 3133)	1.80		18.0	remained in life		
No. 25 (No. 3134)	1.62	1 R.A.U.	16.2	† 2 days	80	(of 8 rabbits)
No. 26 (No. 3135)	1.43		14.3	† 2 "		2.2 days
No. 27 (No. 3136)	1.53		15.3	† 2 "		
No. 28 (No. 3137)	1.33		13.3	† 3 "		
No. 29 (No. 3138)	1.45		14.5	remained in life		
No. 30 (No. 3139)	1.40		14.0	† 3 days		
No. 31 (No. 3140)	1.67		16.7	† 2 days		
No. 32 (No. 3141)	1.50		15.0	† 3 "		
No. 33 (No. 3142)	1.85		18.5	† 3 "		
No. 34 (No. 3143)	1.38		13.8	† 3 "		

No. of rabbits	Body weight (kilos)	Yakriton, subcutaneously used, 1 hour after the administration of phosphorus	Amount of "Nekoirazu" emulsion (0.5%) per os used (c.c.)	Result of experiment (†=death in)	Mortality (%)	Average days of survival (of those dead animals alone)
No. 35 (No. 3144)	1.65	5 R.A.U.	16.5	† 2 days	100	(of 10 rabbits)
No. 36 (No. 3145)	1.35		13.5	† 2 "		2.1 days
No. 37 (No. 3146)	1.43		14.3	† 1 day		
No. 38 (No. 3147)	1.50		15.0	† 2 days		
No. 39 (No. 3148)	1.57		15.7	† 1 day		
No. 40 (No. 3149)	1.50		15.0	† 2 days		
No. 41 (No. 3150)	1.82	50 R.A.U.	18.2	† 2 days	100	(of 5 rabbits)
No. 42 (No. 3151)	1.42		14.2	† 2 "		
No. 43 (No. 3152)	1.57		15.7	† 2 "		2 days
No. 44 (No. 3153)	1.58		15.8	† 2 "		
No. 45 (No. 3154)	1.57		15.7	† 2 "		

TABLE III.

Therapeutic effect of yakriton used after 6 hours in the case of subacute phosphorus poisoning with 0.5% "Nekoirazu" emulsion.

No. of rabbits	Body weight (kilos)	Yakriton, subcutaneously used, 6 hours after the administration of phosphorus	Amount of "Nekoirazu" emulsion (0.5%) per os used (c.c.)	Result of experiment (†=death in)	Mortality (%)	Average days of survival (of those dead animals alone)
No. 1 (No. 3155)	1.48	$\frac{1}{2}$ R.A.U.	14.8	† 2 days	60	(of 6 rabbits)
No. 2 (No. 3156)	1.75		17.5	† 3 "		
No. 3 (No. 3157)	1.60		16.0	remained in life		
No. 4 (No. 3158)	1.70		17.0	"		
No. 5 (No. 3159)	1.42		14.2	† 2 days		
No. 6 (No. 3160)	1.43		14.3	remained in life		2.8 days
No. 7 (No. 3161)	1.37		13.7	† 4 days		
No. 8 (No. 3162)	1.36		13.6	† 2 "		

No. of rabbits	Body weight (kilos)	Yakriton, subcutaneously used, 6 hours after the ad- ministration of phosphorus	Amount of "Nekoirazu" emulsion (0.5%) per os used (c.c.)	Result of experiment (†=death in)	Mor- tality (%)	Average days of survival
No. 9 (No. 3163)	1.50		15.0	remained in life		
No. 10 (No. 3164)	1.45		14.5	† 4 days		
No. 11 (No. 3165)	1.38		13.8	remained in life		
No. 12 (No. 3166)	1.88		18.8	† 2 days		
No. 13 (No. 3167)	1.42		14.2	remained in life		
No. 14 (No. 3168)	1.60		16.0	"		
No. 15 (No. 3169)	1.60	$\frac{1}{4}$ R.A.U.	16.0	† 3 days	70	(of 7 rabbits) 2.7 days
No. 16 (No. 3170)	1.58		15.8	† 2 "		
No. 17 (No. 3171)	1.70		17.0	† 3 "		
No. 18 (No. 3172)	1.70		17.0	† 3 "		
No. 19 (No. 3173)	1.50		15.0	† 2 "		
No. 20 (No. 3174)	1.80		18.0	† 4 "		
No. 21 (No. 3175)	1.60		16.0	remained in life		
No. 22 (No. 3176)	1.43		14.3	† 3 days		
No. 23 (No. 3177)	1.38		13.8	† 4 "		
No. 24 (No. 3178)	1.68		16.8	remained in life		
No. 25 (No. 3179)	1.48	1 R.A.U.	14.8	† 4 days	80	(of 8 rabbits) 2.7 days
No. 26 (No. 3180)	1.38		13.8	† 3 "		
No. 27 (No. 3181)	1.56		15.6	† 2 "		
No. 28 (No. 3182)	1.65		16.5	† 2 "		
No. 29 (No. 3183)	1.32		13.2	† 2 "		
No. 30 (No. 3184)	1.30		13.0	† 2 "		
No. 31 (No. 3185)	1.62		16.2	† 3 days		
No. 32 (No. 3186)	1.55		15.5	† 2 "		
No. 33 (No. 3187)	1.75		17.5	† 3 "		
No. 34 (No. 3188)	1.52		15.2	† 2 "		

No. of rabbits	Body weight (kilos)	Yakriton, subcutaneously used, 6 hours after the administration of phosphorus	Amount of "Nekoirazu" emulsion (0.5%) per os used (c.c.)	Result of experiment (†=death in)	Mortality (%)	Average days of survival
No. 35 (No. 3189)	1.73	5 R.A.U.	17.3	† 3 days	100	(of 10 rabbits) 2.4 days
No. 36 (No. 3190)	2.17		21.7	† 2 "		
No. 37 (No. 3191)	1.83		18.3	† 2 "		
No. 38 (No. 3192)	1.96		19.6	† 2 "		
No. 39 (No. 3193)	1.96		19.6	† 2 "		
No. 40 (No. 3194)	1.25		12.5	† 3 "		
No. 41 (No. 3195)	1.40	50 R.A.U.	14.0	† 2 days	100	(of 5 rabbits) 2 days
No. 42 (No. 3196)	1.45		14.5	† 2 "		
No. 43 (No. 3197)	1.41		14.1	† 2 "		
No. 44 (No. 3198)	1.16		11.6	† 2 "		
No. 45 (No. 3199)	1.54		15.4	† 2 "		

TABLE IV.

Therapeutic effect of different R.A.U. of yakriton and the number of days of survival in the case of subacute phosphorus poisoning.

Approximate number of days of survival	2	2½	3	∞
R.A.U. of yakriton used	50→5 0	1→½ ←	↘½ ↙½ ←.....→½	

As shown in these tables the same number of yakriton units as was effectual in the case of prevention of subacute phosphorus poisoning, was effectual in these therapeutic experiments. And it is strange to say that those rabbits which survived the intoxication appeared quite healthy during the whole time of the experiment. It will appear from the results of the 18th, the 23rd and the present report of yakriton that in the case of $\frac{1}{2}$ or $\frac{1}{4}$ R. A. U., a very effectual combination curve of con- and pro-effects of

yakriton for the detoxication of phosphorus will occur and continue for a rather long period.

Conclusions.

In the prophylactic experiments previously shown a previous injection of $\frac{1}{2}$ R. A. U. or $\frac{1}{4}$ R. A. U. of yakriton was excellently effectual for the detoxication of subacute and acute phosphorus poisoning of rabbits. Now, the present experiment of the therapeutic use of yakriton, has shown the following facts :—

1. If $\frac{1}{2}$ R. A. U. of yakriton is used subcutaneously 3–6 hours after the per oral administration of phosphorus in such an amount as to cause subacute poisoning, it will save almost half the number of animals used, and in an excellent state of health ; while controls with no use of yakriton invariably succumb.

2. Larger numbers of R. A. U. of yakriton show a much less favorable effect ; such a fact was also seen in the case of the prophylactic experiments as previously reported.

The therapeutic use of yakriton for phosphorus poisoning in soluble form was clinically experimented in a child in our department in 1928.¹⁾ Therapeutic use with recovery of yakriton in insoluble form was reported by Ito²⁾; the case was an adult and he was cured.

The third case reported by Dr. Kozo Sato³⁾ was the most interesting. It was a female case of 26 years of age who, probably worried over her long illness—phthisis, tried to commit suicide by means of 5 grams of the “Nekoirazu” (ca. 0.25 grams of phosphorus). The condition was too grave to try a lavage and she was given up as lost by the doctor, who, however, admitted her to his hospital and tried 3 units of insoluble yakriton three times in the course of the treatment. The incident happened in January, 1930 ; the patient is still living up to the time of writing (June 1930).

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1) The paper was read by Yanagawa and Asakura, Febr. 15, 1929 ; published in *Zika Zasshi*, 1930, 1045.

2) T. Ito, *Chiryō Yakuho*, 1930, 334, 33.

3) Personal communication, published in the paper by Yanagawa and Asakura.¹⁾