

Immune Alteration in Rebleeding

Hahn Shick Lee, M.D., Kwang Hyun Cho, M.D., Dae Kon Sohn, M.D., Jun Seok Park, M.D., Jong Ho Lee, M.D., Sung Pil Chung, M.D.¹

Purpose: This study evaluates whether the adaptation mechanism could modulate immunosuppression following a hemorrhage.

Methods: Minor hemorrhage (10% of total blood volume) was induced in the rat model, 1, 2, 4, and 7 days before the main hemorrhage. The immune responses were observed by measuring Con A (Concanavalin A) stimulated proliferative capacity of the peripheral lymphocyte subpopulations, and the Interleukin-2 (IL-2) release from splenocytes.

Results: The proliferative capacity of the splenocytes (SPC) decreased in two days interval model with hemorrhages more than 20% of the total blood volume. The SPC increased in the group with 10% hemorrhage pretreatment 7 days prior to 20% main hemorrhage than it was for 20% or 30% main hemorrhage only with cardiac puncture groups. The SPC increased on the first day than it was on the fourth day after the 20% main hemorrhage, in the pre-treatment group with 7 days interval. The amount of IL-2 release by the splenocytes was higher in the 10~20% group (10% pretreatment hemorrhage and 20% main hemorrhage) than it was in the 0~30% group, when the hemorrhage interval was 7 days, and it was higher on the first day than on the fourth day after the second hemorrhage in the 10~20% group.

Conclusion: The immune response varied depending on the hemorrhage interval following pretreatment, and it increased after the main hemorrhage that, by itself, would

cause immunosuppression. But this effect, however, was only observed during a short period (about 1 day) following the second hemorrhage.

Key Words: Hemorrhage, Immunosuppression, Tolerance

Department of Emergency Medicine,
 Yonsei University College of Medicine, Seoul, Korea,
¹Department of Emergency Medicine, Chungnam
 National University Hospital, Daejeon, Korea

ple organ failure; MOF) (multi
 MOF

가 가
 가 가
 1-4)

24 30 ml/kg
 96 5% 67%
 24 20 ml/kg

Interleukin (IL)-1, Tumor Necrotic Factor (TNF), mRNA 가 6).

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Tel: 02) 3497-3030, Fax: 02) 3462-0713

E-mail: emer6657@yumc.yonsei.ac.kr

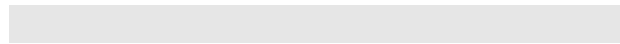
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scintillation vial cocktail (Aquasol-2; Packard, Meriden, CT, USA) 가 liquid scintillation counter (LS 5000 TA; Beckman Instruments, Fullerton, CA, USA)

Con A

가

3.



1.

Dawley 300 ~ 350 g Sprague- . 5% halothane 3% halothane N₂O O₂ . 26G 1/4 75 ml/kg 3

T CD3, T CD4, T CD8, B CD45RA Fluorescein isothiocyanate (FITC) 가, CD8 CD45RA R-phycoerythrin (R-PE) FACS-Calibur (Becton-Dickinson, San Jose, CA, USA) PC-LYSIS

4. IL - 2

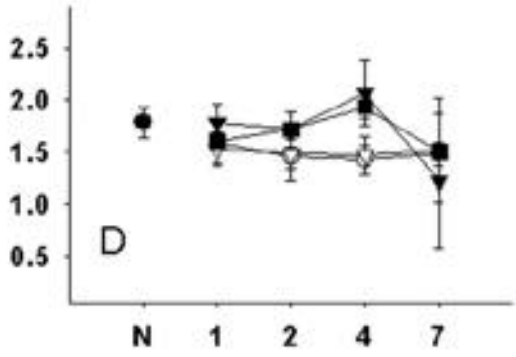
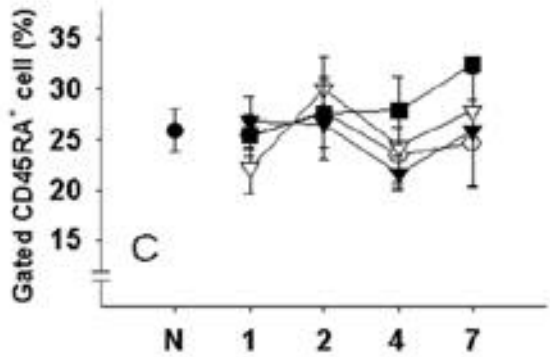
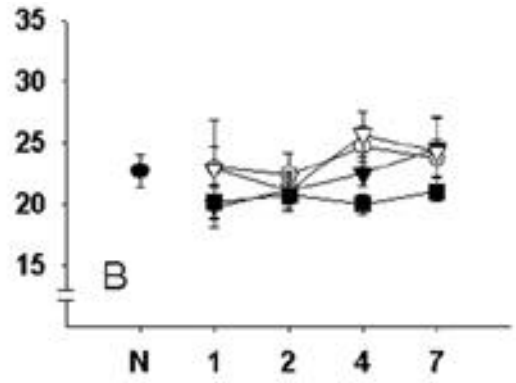
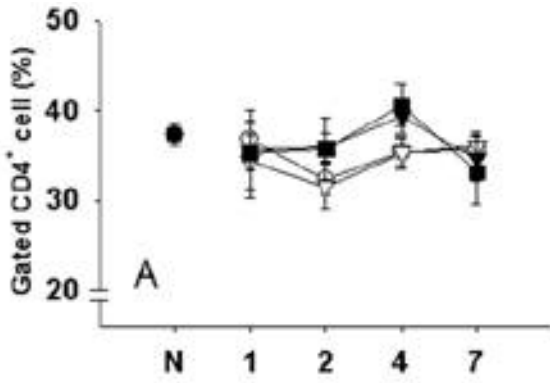
Con A RPMI 1640 (Sigma) 10% (fetal bovine serum, Gibco, Grand Island, NY, USA) 24 IL-2 rat IL-2 Kit (Cytoscreen, Biocource International, Cama-rillo, CA, USA) Strepta-vidin-HRP conjugate 가 4 chromogen 100 μ 가 100 μ stop solution 가 microplate reader (Spectramax 340; Molecular Devices, Sunnyvale, CA, USA) 450 nm IL-2 IL-2

2.

mitogen Con A (Concanavalin A, Sigma, St. Louis, MO, USA, 96 [methyl-3H]-thymidine (NEN, Boston, MA, USA; specific gravity 6.7Ci/mmol) (Skatron Instruments, Sterling, VA, USA) fiber glass filter mat

5.

± SPSS 8.0 Tukey p 0.05



1. 7, A; X (%), B; (/mm³), C; (%), D; (x /mm³). : (N), : 10% (7.5 ml/kg), : 20% (15 ml/kg), : 30% (22.5 ml/kg). *; p<0.05, #; p<0.05, n=8.

2,901, 22,101 ± 4,500, 8,433 ± 2,172 8,118 ± 1,216
cpm 20% 30%
(2, B). 1, 4, 7
가 (2, A, C, D).

1. 1

가.

10,000

CD3+ (pan T) 47.9 ± 4.2%, CD45RA+ (B) 25.9 ± 2.1%, CD4+ (T) 37.3 ± 1.2%, CD8+ (T) 22.7 ± 1.3% , (1, A, B, C). T T CD4+/CD8+ ratio 0.79 ± 0.15 (1, D).

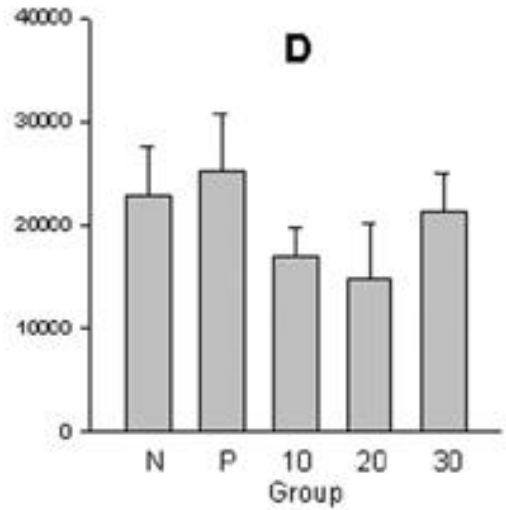
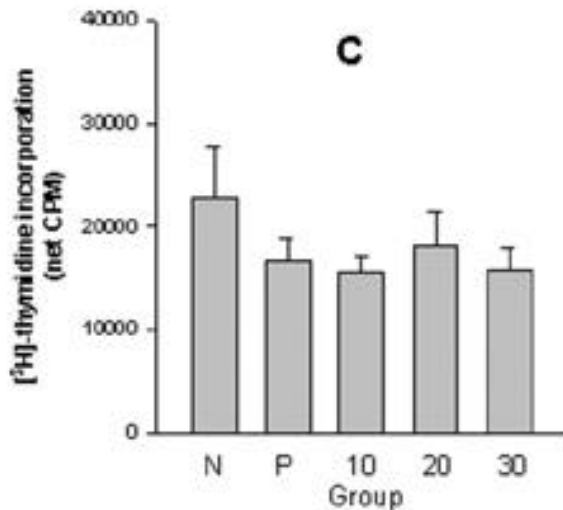
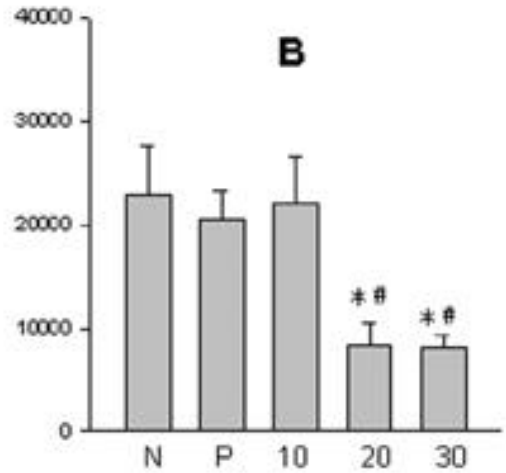
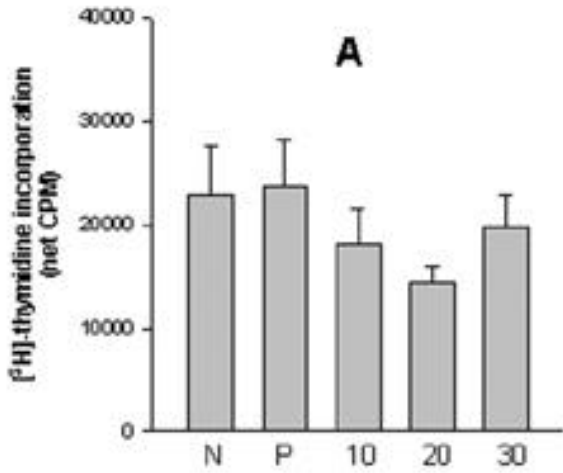
2. 2

가. 10%

10% 2 0%, 10%, 20%, 30%
2 Con A
. 10%~0%, 10~10%, 10~20%
7,138 ± 1,154, 4,992 ± 441 2,987 ± 224 cpm
10~0% 10~20%
(p<0.01, 3). 10%~30%

Con A [3H]-thymi dine incorporation 22,820 ± 4,869 cpm 2 0, 10, 20, 30% 20,456 ±

. 10~20% 10% 20% 1, 2, 4, 7 2 1, 2, 4, 7 2,075 ± 379, 248 ± 557, 710 ± 632,



2. X N: , P: , 10: 10% (7.5 ml/kg), 20: 20% (15 ml/kg), 30: 30% (22.5 ml/kg) , Y [3H]-thymidine incorporation A: 1 , B: 2 , C: 4 , D: 7 . Tukey * ; N p<0.05, # ; P p<0.05. n=8.

7,300±1,608 cpm , 1, 2 7 가 (p<0.01, 4).

Con A (p<0.01, 5, B).

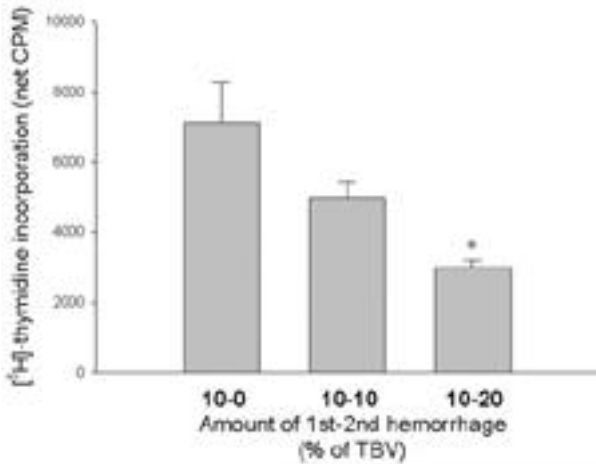
. 10~20% 0~20% 0~30% . 10% 7 20%

20% 2 10% 14,367±6,188 cpm 2 3,158±2,053, 2,468±1,761 cpm 1 가 4 20% 30% 12,445± 1,241 9,229±1,736 cpm 가 (5, A).

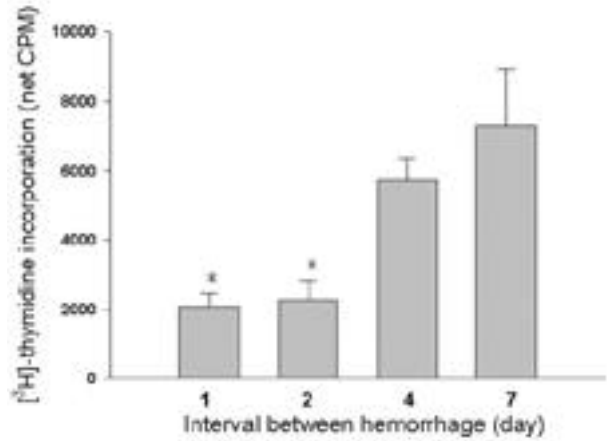
10% 7 20% 1, 2, 4 16,904±4,973, 가 (p<0.05, 6, A).

7 10~20%, 0~20% 0~30% 29,289±6,899, 15,775 ±2,009, 11,410±2,308 cpm 20% 10% 0~20% 0~30%

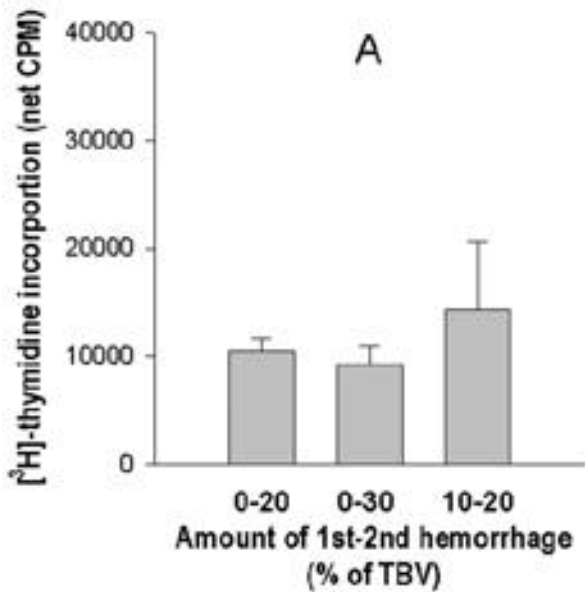
IL-2 2 10~20%, 0~20% 0~30% Con A IL-2 48.6±4.5, 53.4±16.0, 72.1±9.5 pg/ml



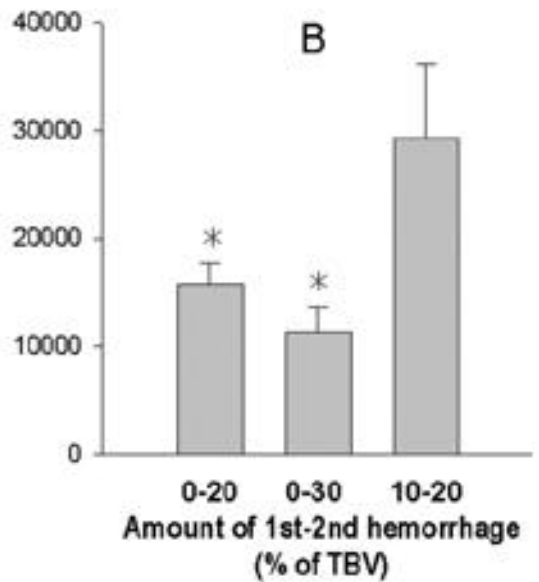
3. 10% 2
 10% 2 0, 10, 20%
 Con A
 10~20% 10~0%
 * : 10~0%
 p<0.01, n=8.



4. 10~20%
 10% 20%
 1, 2, 4, 7
 * ; 7
 p<0.01, n=8.



5. 10~20% 0~20% 0~30%
 0~20% 0~30%
 A:
 B:
 * : 10~20%
 p<0.05,



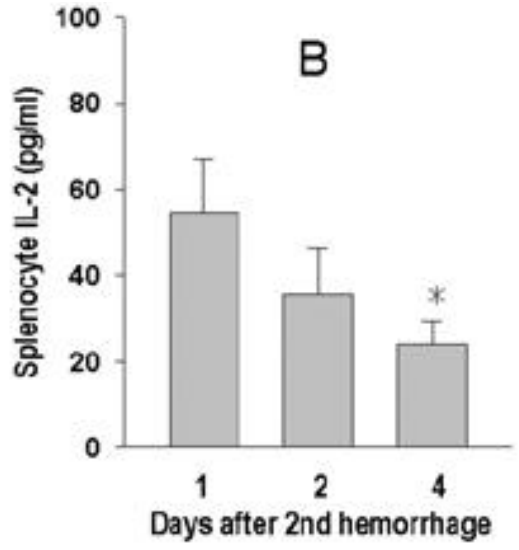
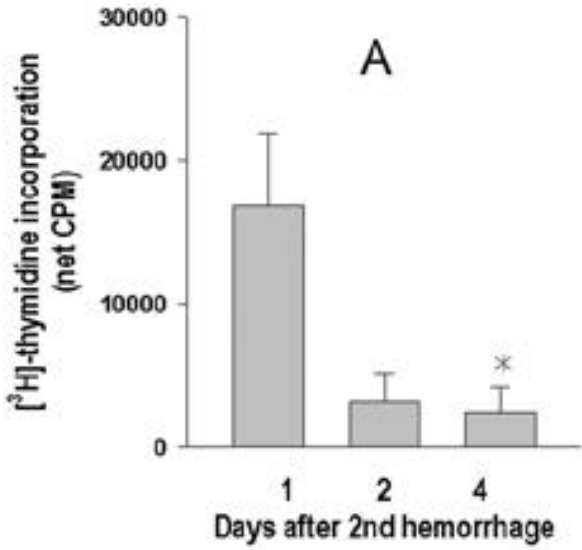
10~20% 2 Con A
 2
 0~20%, 0~30%
 n=8.

가 , 7
 10~20%, 0~20% 0~30% 56.8±5.0,
 41.3±6.5, 84.2±11.5 pg/ml 10~20% 0~30%
 가 (p<0.05, 7).
 10% 7 20% 1, 2, 4
 IL-2 54.7±12.4,
 35.6±10.6, 24.1±5.3 pg/ml 1 가 4

IL-2 (p<0.05, 6,
 B).



1920



6. 10% 7 20%
(B) IL-2 . *: 1

p<0.05, n = 8. (A) Con A

, 'wound factor'

가 . Sauaia ⁷⁾

, 7
61% 가

, Moore ⁸⁾

가 'one-hit' 'two-hit' 가 , 가
(one-hit)

hit) (2nd-

^{9,10)}

¹¹⁾

가

^{12,13)}

, T , B , ,

¹⁴⁾

10, 20, 30%

가
10% (7.5 ml/kg)

83 mmHg, 20% (15 ml/kg) 73
mmHg, 30% (22.5 ml/kg) 45 mmHg, 40% (30
ml/kg) 25 mmHg 40%

30%

35 mmHg

¹⁵⁾

20% (15 ml/kg)

가

30%

48

가 ,

60

2

1

18%

가

가

10

98%

^{1,16)}

1

가

가

가

^{17,18)}

2

20,

30%

가

7

10

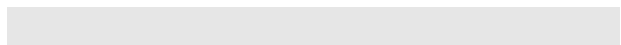
가

7

가

¹⁹⁾

IL-2 가 . IL-2
 1 가 .
 T
 T
 21 가 가 가 IL-2
^{20,21)} 2 가 가 ,
 T 가 ,
 T T 가 ,
²²⁾ 가 T 가
 가 가 가 T T
 가 ²³⁾
 가 Yamashita ²⁴⁾
 10 ml/kg TNF-, mRNA 가 가 . Knoferl ²⁹⁾
 24 48 4 Ringer's
 가 two- 120 30 60
 hit 가 10% 2 4 IL-3 interferon-
 10% 10%~0% IL-1 IL-6 가
 model" 10% " two-hit 7 가
 " " two-hit
 model"
 (neutrophil) 가 가
 (2nd-hit) 6~24
^{25,26)} 2~4 가
 5~8 ³⁰⁾
 가
²⁵⁾
 Claridge ^{27,28)}
 5
 5
 10%
 20%
 1, 2 7
 10% 7 20%
 7 20%
 30% 가
 10% 20% 2
 10% 7 20% 7
 IL-2
 7
 10~20% 0~30%
 0~30% IL-2 가 가 , 10~20% 1
 가 4 IL-2



1. Con A 20% 2 .
2. 20% 7
10%
20% 30% Con A
가 .
3. 10% 7 20% 1, 2, 4
Con A
1 가 4
4. 7 10~20% 0~30%
IL-2 가 가 , 10~20% 1
가 4 IL-2

가가

1

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