Prevalence of Autoantibodies in Thai Elderly

ORRAWADEE HANVIVATVONG, MSc*
YADAH KAOWOPAS, BSc*,
SURANAN TIRAWATNAPONG, MSc*,
SUTTHICHAI JITAPANKUL, MD**

Abstract

To investigate the prevalence of autoantibodies in a normal Thai elderly group, the authors measured anti-thyroid antibodies (anti-thyroglobulin, anti-thyroid microsome), antinuclear antibodies (ANA) and rheumatoid factors (RF) in 429 normal elderly (206 men, 223 women, age range 50-102 years). The participants recruited from Romklao Village, Lat Krabang, a suburb of Bangkok and compared to 219 young normal subjects (110 men, 109 women; age range 19-49 years). The prevalence of anti-thyroid antibodies was significantly increased in the elderly group when compared to the younger age control group (14.69% *vs* 5.02%, p = 0.0005). The antibody titers were found to be higher and the prevalence was more predominant in women than in men both in the elderly (21.53% *vs* 7.28%, p = 0.00005) and control groups (10.09% *vs* 0%, p = 0.0018). The prevalence of ANA in the elderly group was lower (1.17%) when compared to the control group (4.11%). ANA were characterized by low titer of antibodies and several staining patterns, and there was no difference between men and women. For RF, the prevalence was almost the same in both groups (2.79% in the elderly and 2.73% in control group) and no difference was observed. However, when all the three autoantibodies were considered, 20.28 per cent of the elderly individuals were found to have at least one of the autoantibodies which was significantly higher than in the younger control group (11.41%, p = 0.006). The prevalence was more predominant in women than in men. The results from this study can be used as basic data for the evaluation of autoantibodies testing in an elderly Thai population.

Key word : Prevalence, Autoantibodies, Thai Elderly

HANVIVATVONG O, TIRAWATNAPONG S, KAOWOPAS Y, JITAPANKUL S
J Med Assoc Thai 2003; 86 (Suppl 2): S242-S249

* Immunology Unit, Department of Microbiology,
** Gerontology Medicine Unit, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.

Aging is associated with the alteration in the immune functions of both the cellular and humoral immune response. An increase in prevalence of various organ-specific and non-organ-specific autoantibodies is widely demonstrated in the elderly when compared to younger individuals[1-4]. However, the prevalence of each autoantibody varied in other reports, i.e. thyroid antibodies have been reported to have a prevalence of 1 per cent to more than 30 per cent in different ethnic elderly populations[5,6]. To date, no single mechanism has emerged as being responsible for all the observations. It has been hypothesized that these autoantibodies are nonspecifically elevated generally as a result of immunosenescence of the aging process itself, since it is usually unassociated with clinical disease[7]. However, this hypothesis has been challenged by the findings of some investigators that certain autoantibodies were significantly more prevalent in elderly patients with chronic illness or related more to global health status than to the effects of aging[8,9]. Moreover, the prevalence of autoantibody in healthy centenarians was found to have no significant difference from that observed in a younger control aged group[10,11]. Interestingly, other reports have not confirmed the increased prevalence of autoantibodies in elderly individuals[12,13].

Many factors may affect the variability in the prevalence of various autoantibodies i.e. the detection methods, ethnic difference and sex, environmental factors including drugs used, diet, physical activity, underlying disease or exogenous influences of elderly population studies.

In the present study, the authors investigated the prevalence of anti-nuclear antibodies (ANA), rheumatoid factors (RF) and anti-thyroid antibodies, which were among the most clinically utilized autoantibodies in autoimmune disease patients. The difference in the prevalence of these autoantibodies between men and women of different age ranges were also analyzed.

MATERIAL AND METHOD

Participants

Serum specimens of elderly individuals were obtained from participants who were recruited from Lat Krabang, a suburb of Bangkok. The elderly population studied were some of the participants who enrolled in the project of "long-term study of problems, risk of problems and factors of good health status in the elderly who were living in Romklao Village, Lat Krabang, Bangkok" (CERB project). This project was conducted by the Gerontology Medical Unit, Faculty of Medicine, Chulalongkorn University. Sociodemographic background information for all participants (family, social network, education, work, life style and living conditions), medical history, medication use, dietary information, personal health behavior and other health status were obtained by interviewing, laboratory testing (CBC, kidney and liver function tests, lipid profile, electrolyte, etc) and physical examination. Participants who were shown to have any signs and symptoms related to autoimmune diseases were excluded from the study. Four hundred and twenty-nine elderly participants were included in this study. They were 206 males and 223 females with age ranging from 50 to 102 years. (Table 1). For the control, sera from 209 healthy blood donors and medical students, 110 males and 109 females with an age range of 17-49 years, were used as the young controls. All the sera were kept at -70°C before testing.

Method

Anti-thyroid antibodies

Anti-thyroglobulin and anti-thyroid microsomal antibodies were detected by passive hemagglutination assay with the commercial assay kits: Thymune T and Thymune M (Murex Diagnostic

Table 1. Age and sex distribution in the elderly and normal control groups.

Studied group	Number tested		
	Female	Male	Total
Elderly			
50-59	73	75	
60-69	72	75	
70-79	53	43	
80-89	21	13	
90-102	4	0	
Total	223	206	429
Normal control			
17-19	20	20	
20-29	29	30	
30-39	30	30	
40-49	30	30	
Total	109	110	219

Limited, United Kingdom) respectively. The serum was considered positive when antibody titer was equal to or greater than 1 : 20 for anti-thyroglobulin and 1 : 10^2 for anti-thyroid microsomal antibodies.

Antinuclear antibodies

Antinuclear antibodies were detected by an indirect immunofluorescence method using in-house HEp-2 cells as substrate. Patients' sera were diluted 1:20 in phosphate buffered saline (PBS) pH 7.2 and incubated with HEp-2 cells for 30 minutes at room temperature in a moist chamber. The slides were then washed in PBS for a 10 min and incubated with fluorescein conjugated rabbit antihuman immunoglobulin (Dako A/S, Denmark) for a further 30 min followed by 10 min wash in PBS. The slides were counterstained with 0.05 per cent Evan blue for 20 seconds followed by 10 min wash as described above and were then mounted in buffered glycerol and read on a fluorescence microscope. Positive and negative control sera were included in each run. The serum was considered positive when antibody titer was equal to or greater than 1 : 20.

Rheumatoid factors

Rheumatoid factors were detected by using the reagent kit Rapitex® RF (Dade Behring, Germany) which is a qualitative passive latex agglutination assay. The positive result was scored as 1+ to 4+ according to the strength of the reaction and was reported as positive or negative.

Statistical analysis

The results were calculated as percentage of positivity and compared each group by chi-square test or Fisher's exact test, as appropriate.

RESULTS

Thyroid antibodies

Anti-thyroid antibodies (anti-thyroglobulin and anti-thyroid microsomal antibodies) were positive in 63 participants of the 429 elderly group (14.69%) which was significantly higher than the younger age control group (5.02%, p = 0.0005). The prevalence was more predominant in women (48 in 206, 21.53%) than in men (15 in 206,7.28%) in the elderly group. Thirty participants were shown to have only anti-thyroglobulin (6.99% of the elderly group) with an antibody titer varying from 1 : 20 to 1 : 2,560. Eleven participants were found to have only anti-thyroid

Table 2. Prevalence of thyroid antibodies (antithyroglobulin and antithyroid microsome) in the elderly and control groups.

Studied group	No. tested	Anti-T only		Anti-M only		Both anti-T and anti-M		Total		Difference (p)
		No. of positive for thyroid antibodies	%	No. of positive for thyroid antibodies	%	No. of positive for thyroid antibodies	%	No. of positive for thyroid antibodies	%	
Elderly										
Male	206	6	2.91	2	0.97	7	3.39	15	7.28	Male *vs* Female
Female	223	24	10.76	9	4.04	15	6.73	48	21.53	(p = 0.0005)
Total	429	30	6.99	11	2.56	22	5.13	63	14.69	
Normal control										
Male	110	0		0		0		0	0	Male *vs* Female
Female	109	3		5		3		11	10.09	(p = 0.0018)
Total	219	3		5		3		11	5.02	Elderly *vs* Control (p = 0.0005)

microsomal antibodies (2.56% of the elderly group) with the antibody titer varying from 1 : 10^2 to 1 : 80^2.

All 11 of the healthy young control group found to have anti-thyroid antibodies were women. The antibody titer for anti-thyroglobulin ranged from 1 : 20 to 1 : 1,280, and for anti-thyroid microsomal antibodies ranged from 1 : 10^2 to 1 : 40^2. The prevalence of each anti-thyroid antibodies in both groups is shown in Table 2.

Antinuclear antibodies (ANA)

Using in-house HEp-2 cell as substrate, ANA was detected in 1.17 per cent of the sera of the elderly group (5 of 429, 3 men and 2 women). All of them had the antibody titer 1 : 20 which was the cutoff titer of ANA in the present study and the fluorescence patterns were homogenous (in 2 sera), fine speckled and nucleolar in one sera each. Nine (4.11%) sera from 219 of healthy young control group were positive for ANA (3 men and 6 women), the ANA titer ranged from 1 : 20 to 1 : 80 and the fluorescence pattern was homogenous (in 5 sera), nucleolar (in 3 sera) and fine speckled (in 1 sera). No significance difference was seen between men and women with ANA both in the elderly and the control group studied (Table 3).

Rheumatoid factors (RF)

RF was detected in 2.79 per cent of the elderly group (12 of 429, 6 men and 6 women). Similar results were also found in the young control group (2.74%, 6 of 219, 4 men and 2 women). No significance different was seen between men and women with RF in the elderly and the control group studied (Table 3).

Detection of at least one autoantibody in the elderly and young control group

From the 429 elderly population, 87 persons (20.28%) were found to have at least one of the autoantibodies studied (anti-thyroglobulin, anti-thyroid microsome, antinuclear antibodies and rheumatoid factors). Among these, 25 were men (12.14% of elderly men) and 62 were women (27.8% of the elderly women). In the healthy young control group, at least one autoantibody in this study was found in 25 of 219 (11.42%) of this group, 7 were men (6.3% of male control) and 18 (16.51% of female controls) (Table 4). The prevalence of autoantibodies was significantly greater in females when compared to males both in the elderly and the healthy young control ($p = 0.0009$ for elderly group and $p = 0.0316$ for control group). The elderly population was also found to have significantly higher prevalence of autoantibodies when compared to the control group ($p = 0.006$) (Table 4). The details of positive for at least one autoantibody in a different age range both in the elderly and control groups are shown in Table 5.

DISCUSSION

It is generally found that elderly individuals frequently have increased autoantibodies in their sera [1-4] and women usually have a higher prevalence

Table 3. Prevalence of antinuclear antibodies (ANA) and rheumatoid factors (RF) in the elderly and control groups.

Studied group	No. tested	ANA		Difference (p)	RF		Difference (p)
		No. of positive	%		No. of positive	%	
Elderly							
Male	206	3	1.46	M *vs* F	6	2.92	M *vs* F
Female	223	1	0.45	NS (p = 0.93)	6	2.69	NS (p = 0.88)
Total	429	5	1.17		12	2.79	
Normal control							
Male	110	3	2.72	M *vs* F	4	3.64	M *vs* F
Female	109	6	5.50	NS (p = 0.24)	2	1.83	NS (p = 0.35)
Total	219	9	4.11	Elderly *vs* Control (p = 0.02)	6	2.73	Elderly *vs* Control NS (p = 0.83)

M = male, F = female, NS = not significance

Table 4. Detection of at least one autoantibody (anti-thyroid antibodies, antinuclear antibodies or rheumatoid factors) in the elderly and control groups.

Studied group	No. tested	No. of positive	%	Difference (p)
Elderly				
Male	206	25	12.14	Male *vs* Female
Female	223	62	27.80	(p = 0.00009)
Total	429	87	20.28	
Normal control				
Male	110	7	6.36	Male *vs* Female
Female	109	18	16.51	(p = 0.0316)
Total	219	25	11.42	Elderly *vs* Control (p = 0.006)

Table 5. Detection of at least one autoantibody (anti-thyroid antibodies, antinuclear antibodies or rheumatoid factors) in different age ranges of the elderly and control groups.

Age range (yr)	Male			Female			Total positive	%
	No. tested	No. positive	%	No. tested	No. positive	%		
Elderly								
50-59	75	5	6.67	73	22	30.14	27	18.24
60-69	75	11	14.67	72	19	26.39	30	20.41
70-79	43	6	13.95	53	11	20.75	17	17.71
80-89	13	3	23.07	21	9	42.86	12	35.29
90-102	0	0	0	4	1	25.00	1	25.00
Total	206	25	12.14	223	62	27.80	20.28	
Difference M *vs* F					(M *vs* F p = 0.00009)			
Control								
17-19	20	1	4.00	20	2	10.00	3	7.5
20-29	30	1	3.33	29	5	17.24	6	10.17
30-39	30	3	10.00	30	7	23.33	10	16.67
40-49	30	2	6.67	30	4	13.33	6	10.01
Total	110	7	6.36	109	18	16.51	25	11.42
Difference M *vs* F					(M *vs* F p = 0.003)			

M = male, F = female

than men[1,14-15]. However, the prevalence was varied in different studies. Thyroid antibodies, which was reported to have a high prevalence in most elderly populations[5,6], were completely absent in an elderly sub-Saharan African population[16]. This may be the result of different techniques employed to measure the antibodies, ethnic and sex differences, health status of the population studied and environmental factors.

In the present study, the prevalence of anti-thyroid antibodies were found to be significantly increased in elderly subjects when compared to the younger age control group (14.69% *vs* 5.02%, p = 0.005) similar to previous reports[1-6]. The antibodies titers were shown to be higher in the elderly subjects and women had a significantly higher prevalence than men both in the elderly (21.53% *vs* 7.28%, p = 0.00005) and younger age control group (10.09% *vs*

0%, p = 0.0018). Antithyroglobulin was more predominant than anti-thyriod microsomal antibodies (6.99% *vs* 2.56%) which is similar to the report of Gordin et al[17] who also found a higher prevalence of antithyroglobulin than antithyriod microsomal antibodies in asymptomatic autoimmune thyroiditis.

The prevalence of ANA in the present study was considered to be very low (1.17%) when compared to previous reports which mostly detected ANA from 5 per cent up to more than 30 per cent[14,16,18]. All of the elderly individuals who were positive for ANA had a low antibody titer (1 : 20) and several staining patterns were found as seen in other reports [19,20]. There was no significant difference between the prevalence in men and women in both the elderly and younger control group. The prevalence of ANA in the younger age control group was found slightly higher than the elderly group (4.11% *vs* 1.17%, p = 0.02). However, this figure is not considered abnormal when compared to the range of ANA titer in healthy individuals[21].

The authors also found a low prevalence of RF in the elderly individuals in the present study and was presented in only 2.79 per cent which was about the same figure as seen in the control group (2.73%). This is quite different from other reports which found that RF was the most frequent autoantibody in the elderly subjects and they described a prevalence from 9 per cent to 41 per cent[16,18,19,22-24].

The difference between the presented data especially in ANA and RF may be related to several factors as stated earlier. Aside from the ethnicity, the immune status of the subjects studied has been pointed out as an important factor that may affect the prevalence of autoantibodies in the elderly subjects. Juby et al[8,9] found that ANA, RF, together with antibody to double-stranded DNA, and anti-cardiolipin antibodies which has been reported in a very high prevalence in other studies[18,22] was not statistically significantly increased in successfully aging elderly compared to the healthy young controls. A significant increase was seen only in the chronically ill or rheumatoid arthritis sufferers. They concluded that the clinical significance of autoantibodies in elderly patients is related more to global health status than to the effect of aging. The elderly subjects in the present study could be classified as successfully healthy elderly since those who had no signs or symptoms related to autoimmune condition were excluded from the studied.

However, when the overall of the three autoantibodies in the present study were considered, 20.28 per cent of the elderly population were found to have at least one autoantibody which was significantly higher than the younger control group (11.42%, p = 0.006). Therefore, it is likely that immunosenescence may still play a role in the increased prevalence of autoantibodies in these individuals.

The authors could not demonstrate the decreasing prevalence of autoantibodies in the elderly after the ninth decade of life (Table 5) as shown by other investigators who showed that in healthy centenarians the prevalence of autoantibodies was decreased to a level that was not different from that observed in younger age controls[10], especially for the organ specific anti-thyroglobulin and anti parietal cell antibodies[11]. However, the number of very old subjects in this study was too small (4 females) to conclude this difference.

Although only three autoantibodies are investigated in the present study, these autoantibodies are among the most clinically utilization in autoimmune diseases. Therefore, the results from the present study can be used as a basic data for the evaluation of autoantibodies testing in elderly Thai populations.

ACKNOWLEDGEMENTS

The authors wish to thank the elderly participants, blood donors and medical students for their cooperation, Ms. Pranee Srisuparp for her technical assistance. This study was supported by the Rachadapisek Sompoj China Medical Board Funds, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand.

(Received for publication on April 21, 2003)

REFERENCES

1. Hackett E, Beech M, Forbes IJ. Thyroglobulin antibodies in patients without clinical disease of the thyroid gland. Lancet 1960; ii: 402-4.
2. Hijmans W, Radl J, Botazzo GF, Doniach D. Autoantibodies in highly aged humans. Mech Ageing Dev 1984; 26: 83-9.
3. Tomer YK, Shonfeld Y. Aging and autoantibodies. Autoimmunity 1988; 1: 141-9.
4. Goodwin JS, Searles RP, Tung SK. Immunological responses of a healthy elderly population. Clin Exp Immunol 1982; 48: 403-10.
5. Robuschi G, Safran M, Braverman LE, Gnudi A, Roti E. Hypothyroidism in the elderly. Endocrine Reviews 1987; 8: 142-53.
6. Roti E, Gardini E, Minelli R, Bianconi L, Braverman LE. Prevalence of anti-thyroid peroxidase antibodies in serum in the elderly: Comparison with other tests for anti-thyroid antibodies. Clin Chem 1992; 38/1: 88-92.
7. Makidonan T, Kay MMB. Age influence of the immune system. Adv Immunol 1980; 29: 193.
8. Juby AG, Davis P, McElhaney JE, Gravenstein S. Prevalence of selected autoantibodies in different elderly subpopulations. Br J Rheumatol 1994; 33: 1121-4.
9. Juby AG, Davis P. Prevalence and disease associations of certain autoantibodies in elderly patients. Clin Invest Med 1998; 21: 4-11.
10. Mariotti S, Sansoni P, Barbesino G, et al. Thyroid and other organ-specific autoantibodies in healthy centenarians. Lancet 1992; 339: 1506-8.
11. Candore G, Di Lorenzo G, Mansueto P, et al. Prevalence of organ-specific and non organ-specific autoantibodies in healthy centenarians. Mech Ageing Dev 1997; 94: 183-90.
12. Pandey PJ, Fudenberg HH, Ainsworth SK, Loadholt BC. Autoantibodies in healthy subjects of different age groups. Mech Ageing Dev 1979; 10: 399-404.
13. Gordon J, Rosenthal M. Failure to detected age related increase in non-pathological autoantibodies. Lancet 1984; i: 231.
14. Jacobs A, Entwistle CC, Campbell H, Waters WE. A random sample from Wales. IV Circulating gastric and thyroid antibodies and antinuclear factor. Brit J Haemat 1969; 17: 589-95.
15. Couchman KG, Wigley RD, Prior IAM. Autoantibodies in the Carterton population survey. J Chron Dis 1970; 23: 45.
16. Njemini R, Meyers I, Demanet C, et al. The prevalence of autoantibodies in an elderly sub-Saharan African population. Clin Exp Immunol 2002; 127: 99-106.
17. Gordin A, Lamberg BA. Natural course of symptomless autoimmune thyroiditis. Lancet 1975; ii: 1234-7.
18. Manoussakis MN, Tzioufas AG, Silis MP, et al. High prevalence of anti-cardiolipin and other autoantibodies in a healthy elderly population. Clin Exp Immunol 1987; 69: 557-65.
19. Ruffati A, Rossi L, Calligaro A, et al. Autoantibodies of systemic rheumatic diseases in the healthy elderly. Gerontology 1990; 36: 104-11.
20. Moulias R, Proust J, Wang A, et al. Age related increase in autoantibodies. Lancet 1984; i: 1128-9.
21. Tan EM, Feltkamp TE, Smolen JS, et al. Range of antinuclear antibodies in "healthy" individuals. Arthritis Rheum 1997; 40: 1601-11.
22. Roderick AF, Hala T, Robert PS, Arthur DB. The prevalence of anticardiolipin antibodies in a healthy elderly population and its association with antinuclear antibodies. J Rheumatol 1989; 16: 623-5.
23. Teo SK, Soon PC, Ng SC. Autoantibodies in the hospitalised oriental elderly. Singapore Med J 1995; 36: 609-11.
24. Olujide-Oyeyinka G, Samusa-Salimonu L, Olufunmilayo-Ogunsile M. The role of circulating immune complexes: Antinuclear and rheumatoid factor autoantibodies in aging in Nigerians. Mech Ageing Dev 1995; 85: 73-81.

การศึกษาความชุกของออโตแอนติบอดีย์ในคนไทยสูงอายุ

อรวดี หาญวิวัฒน์วงศ์, วทม, สุรนันท์ ตีระวัฒนพงษ์, วทม*,*
ญดา แก้วโอภาส, วทบ, สุทธิชัย จิตะพันธ์กุล, พบ***

ในการศึกษาความชุกของออโตแอนติบอดีย์ในผู้สูงอายุปกติของไทย คณะผู้วิจัยได้ทำการตรวจหา anti-thyroid antibodies (anti-thyroglobulin, anti-thyroid microsome), antinuclear antibodies (ANA) และ rheumatoid factors (RF) ในน้ำเหลืองผู้สูงอายุที่อาศัยในชุมชนรมเกล้า เขตลาดกระบัง กรุงเทพมหานคร จำนวนทั้งสิ้น 429 คน เป็นชาย 206 คน หญิง 223 คน อายุระหว่าง 50-102 ปี เปรียบเทียบกับน้ำเหลืองจากคนปกติที่มีอายุต่ำกว่า 50 ปี จำนวนทั้งสิ้น 219 คน เป็นชาย 110 คน, หญิง 109 คน อายุ 19-49 ปี พบว่าในผู้สูงอายุของไทย มีอัตราการตรวจพบ anti-thyroid antibodies สูงกว่ากลุ่มควบคุมที่มีอายุน้อยกว่าอย่างมีนัยสำคัญทางสถิติ (14.69% *vs* 5.02%, p = 0.0005) โดยเพศหญิงมีอัตราการพบแอนติบอดีย์นี้สูงกว่าในเพศชายทั้งในกลุ่มผู้สูงอายุ (21.53% *vs* 7.28%, p = 0.00005) และกลุ่มควบคุม (10.09% *vs* 0%, p = 0.0018) ส่วนอัตราการพบ ANA ในผู้สูงอายุค่อนข้างต่ำ (1.17%) เมื่อเปรียบเทียบกับกลุ่มควบคุม (4.11%) และระดับแอนติบอดีค่อนข้างต่ำ อัตราในเพศหญิงไม่ต่างจากในเพศชายทั้งสองกลุ่ม สำหรับ RF นั้น พบในอัตราที่ใกล้เคียงกันทั้งในกลุ่มผู้สูงอายุ (2.79%) และกลุ่มควบคุม (2.73%) และไม่มีความแตกต่างระหว่างเพศในการพบ RF นี้ อย่างไรก็ตามเมื่อวิเคราะห์ถึงการตรวจพบออโตแอนติบอดีย์อย่างใดอย่างหนึ่งอย่างน้อย 1 ชนิดแล้ว พบว่าในกลุ่มผู้สูงอายุมีความชุกสูงกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ (20.28% *vs* 11.41%, p = 0.006) นอกจากนั้นในแต่ละกลุ่มยังพบว่าเพศหญิงมีอัตราการพบออโตแอนติบอดีย์ที่สูงกว่าในเพศชาย ผลวิจัยที่ได้นี้สามารถใช้เป็นข้อมูลพื้นฐานสำหรับการใช้ประกอบการพิจารณาแปลผลการทดสอบออโตแอนติบอดีย์ต่าง ๆ ในผู้สูงอายุของไทย

คำสำคัญ : ความชุก, ออโตแอนติบอดีย์, ผู้สูงอายุไทย

อรวดี หาญวิวัฒน์วงศ์, สุรนันท์ ตีระวัฒนพงษ์,
ญดา แก้วโอภาส, สุทธิชัย จิตะพันธ์กุล
จดหมายเหตุทางแพทย์ ฯ 2546; 86 (ฉบับพิเศษ 2): S242-S249

* หน่วยวิทยาภูมิคุ้มกัน, ภาควิชาจุลชีววิทยา,
** สาขาวิชาเวชศาสตร์ผู้สูงอายุ, ภาควิชาอายุรศาสตร์, คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย, กรุงเทพ ฯ 10330