นิพนธ์ต้นฉบับ

Changes in sera biochemistry and hormones in elderly Thai subjects : a preliminary report.

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A test panel of 11 biochemicals and five hormones was studied in elderly Thai Subjects aged 50-89 years. They comprised 123 males and 127 females divided into four groups according to the Subjects' age. The results in each group were compared with those obtained from 30 male and female subjects of reproductive age. It was found that the alkaline phosphatase, cholesterol, glucose and uric acid levels increased with age, while the concentration of total bilirubin decreased. Albumin showed a slight decrease with age. Total protein did not change with age. Calcium in elderly males increased compared with males of reproductive age. The results suggest that it would be necessary to set up reference values for biochemical substances in elderly subjects as part of health care services for these people.

The levels of FSH in elderly females were found to be between 40 and 60 IU/L, while LH showed a fairly constant level of 30 IU/L, which is twice as high as the level in women of reproductive age. The levels of both these hormones in elderly males were each about 10 IU/L. Testosterone levels in elderly male subjects between the ages of 50 and 79 years were fairly constant at 17 nmol/L, decreasing to 14 nmol/L in subjects over 80 years of age. Most of the estradiol in elderly women could not be measured, unlike one fifth of the elderly male subjects who showed an estradiol level of 200-300 pmol/L. This finding suggests that the measurement of estradiol might not be a valuable index for the study of estrogen changes in elderly females.

Key words : Elderly Thai biochemical substances, hormones

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ได้ทำการศึกษาสารชีวเคมี 11 ชนิด และฮอร์โมนอีก 5 ชนิด ในผู้สูงอายุไทย อายุระหว่าง 50-89 ปี เป็นชาย 123 คน หญิง 127 คน แบ่งออกเป็น 4 กลุ่มอายุ เปรียบเทียบกับชายและหญิงที่อยู่ในวัยเจริญพันธุ์ กลุ่มละ 30 คน พบว่าระดับ alkaline phosphatase, BUN, cholesterol, glucose และ uric acid เพิ่มตามอายุ ส่วน bilirubin มีระดับลดลง และ albumin มีระดับลดลงเล็กน้อยเมื่ออายุมากขึ้น total protein ไม่เปลี่ยนแปลงตามอายุ ระดับ calcium ของชายสูงอายุ มีค่าสูงกว่าชายวัยเจริญพันธุ์ จากผลการวิจัยพอจะสรุปได้ว่าจำเป็นต้องมีค่าอ้างอิงสารชีวเคมีของผู้สูงอายุไทย เพื่อการนำไปใช้บริบาลผู้สูงอายุได้อย่างมีประสิทธิภาพ

ระดับฮอร์โมน FSH ของหญิงสูงอายุมีค่าระหว่าง 40-60 IU/L ส่วนระดับ LH มีค่าค่อนข้างคงที่ระหว่าง 30 IU/L ซึ่งสูงกว่าหญิงที่อยู่ในวัยเจริญพันธุ์ ระดับฮอร์โมนทั้งสองนี้ ในชายสูงอายุมีค่าประมาณ 10 IU/L ชายกลุ่มอายุ 50-79 ปี มีระดับ testosterone ค่อนข้างคงที่ คือประมาณ 17 nmol/L และจะลดลงเป็น 14 nmol/L เมื่ออายุ 89 ปี ระดับ estradiol ในหญิงสูงอายุไม่สามารถจะวัดได้ ซึ่งต่างจากชายสูงอายุพบว่า 1/5 ของชายสูงอายุที่ศึกษา พบระดับ estradiol ประมาณ 200-300 pmol/L ในหญิงสูงอายุเป็นการยากที่จะศึกษาการเปลี่ยนแปลงระดับฮอร์โมน estradiol ในเลือด

The elderly comprise a population in need of good managment for health care; this becomes especially important since the size of this population continues to increase.[1] Therefore, it is essential that basic medical knowledge regarding this population be compiled.

Basic biochemical data nowadays are available on the young and people in the reproductive age group (15-49 years). There is a controversy about the biochemical values reported by several investigators.[2] The values of biochemical substances in people of reproductive age show little biological variation during the ages of 30-50 years.[2] Some investigators[3] have found that three groups of subjects, 18-35 years of age, 36-55 years and more than 56 years, demonstrated small changes in the levels of biochemical substances in people of older ages. Some researchers have found levels of albumin and protein in males to be higher than those in women,[4] while others reported both compounds were lower in those of advancing age.[5] Some invertigators have found the level of alkaline phosphatase in subjects 65-80 years of age to be higher than in those 35-50 years[6] of age, while others found that this enzyme showed no correlation with age in males.[7] Yendt et al.[8] found that the total serum calcium level in females decreased after the age of 65. However, Fraser et al.[9] found that biochemical substances changed in subjects over 70 years of age.

Normally, the study of biochemical changes for the management of elderly Thai subjects is compared with people of reproductive age. All of the above data were obtained from the study of a Caucasian population. However it is inappropriate to use the same data for the medical care of elderly Thai subjects. Therefore, we studied a test panel of 11 biochemicals and five hormones in the sera of elderly Thai subjects.

Materials and Methods

Subjects and specimens

Healthy Thai males females were selected from Pramongkutklao Hospital and divided into two age groups. One group of 30 reproductive age subjects comprised female nurses 18-20 years of age and male soldiers 18-25 years. Elderly subjects, determined by clinicians to be apparently healthy, and who had no indication of disease and had not taken any drugs that would interfere with biochemical substances and hormones, were selected from the Geriatrics Clinic to form the second group. The elderly subjects ranged in age between 50 and 89 years, i.e. 123 males between 80 and 82 years and 127 females who were subdivided by age group as shown in Table 1.

Table 1. Age of the subjects.

Age (yrs.)	Males		Females	
	Range	X ± SD	Range	X ± SD
18 – 25 (G1)	18 – 25 (n = 30)	–	18 – 20 (n = 30)	–
50 – 59 (G2)	54 – 59 (n = 9)	57.66 ± 1.67	51 – 59 (n = 11)	56.45 ± 2.98
60 – 69 (G3)	60 - 69 (n = 79)	64.38 ± 2.92	60 – 69 (n = 91)	63.90 ± 2.82
70 – 79 (G4)	70 – 77 (n = 30)	73.17 ± 2.44	70 – 77 (n = 20)	73.55 ± 2.49
80 – 89 (G5)	81 – 85 (n = 5)	83.00 ± 1.58	80 – 82 (n = 5)	81.20 ± 0.84

Blood specimens from fasting subjects were collected between 9.00 and 11.00 a.m. Sera were separated by centrifugation, after which the blood specimens were left one hours at room temperature and then stored at −20°C until the time of analysis, except for analysis of the labile analytes, e.g. bilirubin, which had to be performed immediately.

Analytical methods

An autoanalyser, SMA II, was used to measure albumin (Alb.), alkaline phosphatase (Alk.), total bilirubin (Bil.), blood urea nitrogen (BUN.), calcium (Cal.), cholesterol (Chol.), creatinine (Crea.), glucose (Glu.), inorganic phosphate (In. phos.), total protein (Total pro.) and uric acid. The coefficient of variation of the interassay was found to be 5.77%, 15.03%, 17.55%, 17.8%, 8.33%, 6.85%, 4.61%, 10.58%, 3.80% and 8.7%, respectively.

Five hormones, namely: prolactin (PRL), follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone (T) and estradiol (E_2), were measured, utilizing the method and materials from the WHO Matched Reagent Programme. The accuracy and precision of the hormone assays were comparable with the procedure as previously described.[10]

Results

Biochemical data

Tables 2, 3 and 4 show the values of the biochemical substances and hormones of the reproductive age males and females and the elderly subjects; figures 1 and 2 show the mean values. The levels of BUN, calcium and glucose of reproductive age males were not determined since there were not enough specimens for analysis.

Table 2. Biochemical data of reproductive age subjects.

Biochemical	Age (18 − 25 years)	
Substances	**Males**	**Females**
Alb. (gm/L)	51.39 ± 3.08 (n = 28)	50.60 ± 7.11 (n = 25)
Alk.phos. (U/L)	49.46 ± 11.82 (n = 28)	66.53 ± 14.06 (n = 30)
Total bil. (mmol/L)	16.75 ± 8.46 (n = 28)	12.52 ± 6.44 (n = 25)
BUN (mmol/L)	—	3.29 ± 0.88 (n = 30)
Cal. (mmol/L)	—	2.47 ± 0.09 (n = 30)
Chol. (mmol/L)	5.02 ± 0.85 (n = 28)	5.18 ± 0.79 (n = 30)
Crea. (mmol/L)	101.5 ± 9.43 (n = 28)	68.37 ± 5.89 (n = 30)
Glu. (mmol/L)	—	4.13 ± 0.41 (n = 30)
In. phos. (mmol/L)	2.46 ± 0.10 (n = 28)	1.39 ± 0.13 (n = 30)
Total pro. (gm/L)	79.11 ± 3.50 (n = 28)	81.76 ± 4.01 (n = 25)
Uric acid (mmol/L)	365.43 ± 47.73 (n = 28)	287.57 ± 55.36 (n = 30)

Table 3. Biochemical data of elderly subjects.

Biochemical	Age (yrs.)							
	50 – 59		60 – 69		70 – 79		80 – 89	
Substances	Males	Females	Males	Females	Males	Females	Males	Females
Alb. (gm/L)	46.6 ± 1.82 (n = 5)	44.75 ± 3.62 (n = 8)	47.2 ± 3.62 (n = 49)	47.34 ± 4.75 (n = 56)	45.91 ± 3.74 (n = 21)	45.29 ± 3.70 (n = 17)	43.33 ± 2.08 (n = 3)	41.00 ± 4.97 (n = 4)
Alk.phos. (U/L)	87.17 ± 48.28 (n = 3)	103.5 ± 28.62 (n = 10)	93.54 ± 27.5 (n = 63)	96.19 ± 23.33 (n = 74)	83.04 ± 22.29 (n = 23)	98.94 ± 42.92 (n = 17)	83.0 ± 26.47 (n = 4)	111.8 ± 41.54 (n = 5)
Bil. (mmol/L)	17.33 ± 4.04 (n = 3)	8.6 ± 4.22 (n = 5)	12.35 ± 4.79 (n = 40)	8.55 ± 4.16 (n = 44)	12.82 ± 5.34 (n = 17)	9.54 ± 3.95 (n = 17)	5 (n = 1)	6.00 ± 2.00 (n = 3)
BUN (mmol/L)	6.13 ± 2.53 (n = 6)	4.57 ± 1.34 (n = 11)	4.78 ± 1.34 (n = 69)	4.79 ± 1.68 (n = 86)	4.82 ± 1.56 (n = 30)	5.08 ± 1.37 (n = 18)	5.89 ± 1.68 (n = 4)	5.70 ± 1.46 (n = 5)
Cal. (mmol/L)	2.53 ± 0.05 (n = 5)	2.45 ± 0.14 (n = 11)	2.43 ± 0.17 (n = 61)	2.41 ± 0.15 (n = 72)	2.40 ± 0.17 (n = 25)	2.32 ± 0.11 (n = 11)	2.37 ± 0.06 (n = 3)	2.55 ± 0.13 (n = 5)
Chol. (mmol/L)	5.78 ± 1.09 (n = 7)	6.34 ± 1.1 (n = 11)	6.1 ± 0.96 (n = 75)	6.51 ± 1.12 (n = 89)	5.83 ± 1.02 (n = 30)	5.42 ± 1.13 (n = 18)	5.77 ± 1.11 (n = 4)	6.99 ± 1.64 (n = 5)
Crea. (mmol/L)	116.83 ± 48.77 (n = 6)	79.27 ± 11.93 (n = 11)	103.76 ± 18.52 (n = 72)	80.83 ± 15.89 (n = 87)	105.28 ± 19.04 (n = 29)	85.94 ± 15.74 (n = 17)	115.75 ± 23.23 (n = 4)	91.00 ± 21.86 (n = 5)
Glu. (mmol/L)	7.08 ± 4.15 (n = 5)	5.1 ± 0.73 (n = 11)	6.0 ± 2.27 (n = 73)	5.77 ± 1.41 (n = 90)	5.64 ± 0.82 (n = 30)	5.86 ± 1.30 (n = 19)	5.08 ± 0.53 (n = 4)	5.62 ± 0.45 (n = 5)
In.phos. (mmol/L)	1.33 ± 0.09 (n = 4)	1.51 ± 0.4 (n = 9)	1.42 ± 1.25 (n = 57)	1.35 ± 0.23 (n = 66)	1.28 ± 0.24 (n = 26)	1.33 ± 0.17 (n = 14)	1.34 ± 0.18 (n = 3)	1.29 ± 0.12 (n = 4)
Total pro. (gm/L)	80.6 ± 2.07 (n = 5)	76.63 ± 4.24 (n = 8)	78.16 ± 4.97 (n = 51)	78.07 ± 5.02 (n = 60)	77.77 ± 6.40 (n = 22)	75.76 ± 3.6 (n = 17)	81.33 ± 6.35 (n = 3)	77.00 ± 4.97 (n = 4)
Uric acid (mmol/L)	470.6 ± 124.33 (n = 5)	313.36 ± 86.92 (n = 11)	399.8 ± 91.58 (n = 70)	351.36 ± 82.62 (n = 85)	403.41 ± 83.37 (n = 29)	329 ± 88.31 (n = 18)	422.25 ± 66.28 (n = 4)	375.80 ± 69.78 (n = 5)

Table 4. Hormonal levels of the elderly subjects.

Biochemical	Age (yrs.)							
	50 – 59		60 – 69		70 – 79		80 – 89	
Substances	Males	Females	Males	Females	Males	Females	Males	Females
PRL (mU/L)	215.6 ± 17.76 (n = 5)	339.7 ± 151.41 (n = 10)	290.49 ± 161.48 (n = 72)	245.52 ± 96.01 (n = 81)	261.00 ± 81.65 (n = 25)	313.25 ± 135.81 (n = 20)	305.00 ± 48.48 (n = 4)	296.40 ± 121.54 (n = 5)
FSH (U/L)	6.18 ± 1.96 (n = 6)	42.63 ± 22.99 (n = 10)	7.73 ± 7.53 (n = 70)	54.58 ± 23.96 (n = 83)	7.84 ± 6.91 (n = 25)	51.35 ± 25.46 (n = 20)	9.74 ± 6.45 (n = 5)	61.22 ± 25.19 (n = 6)
LH (U/L)	9.93 ± 7.07 (n = 7)	28.34 ± 13.57 (n = 11)	9.69 ± 5.45 (n = 72)	32.45 ± 17.21 (n = 87)	10.49 ± 5.02 (n = 27)	29.96 ± 15.04 (n = 19)	13.67 ± 7.33 (n = 5)	32.95 ± 19.65 (n = 5)
T (mmol/L)	17.44 ± 8.8 (n = 8)	—	16.71 ± 5.73 (n = 62)	—	16.96 ± 5.22 (n = 23)	—	13.69 ± 5.53 (n = 5)	—
E_2 (pmol/L)	157.71 ± 38.57 (n = 2)	—	208.2 ± 239.73 (n = 12)	—	186.45 ± 110.71 (n = 6)	—	2.37 ± 0.06 (n = 3)	—

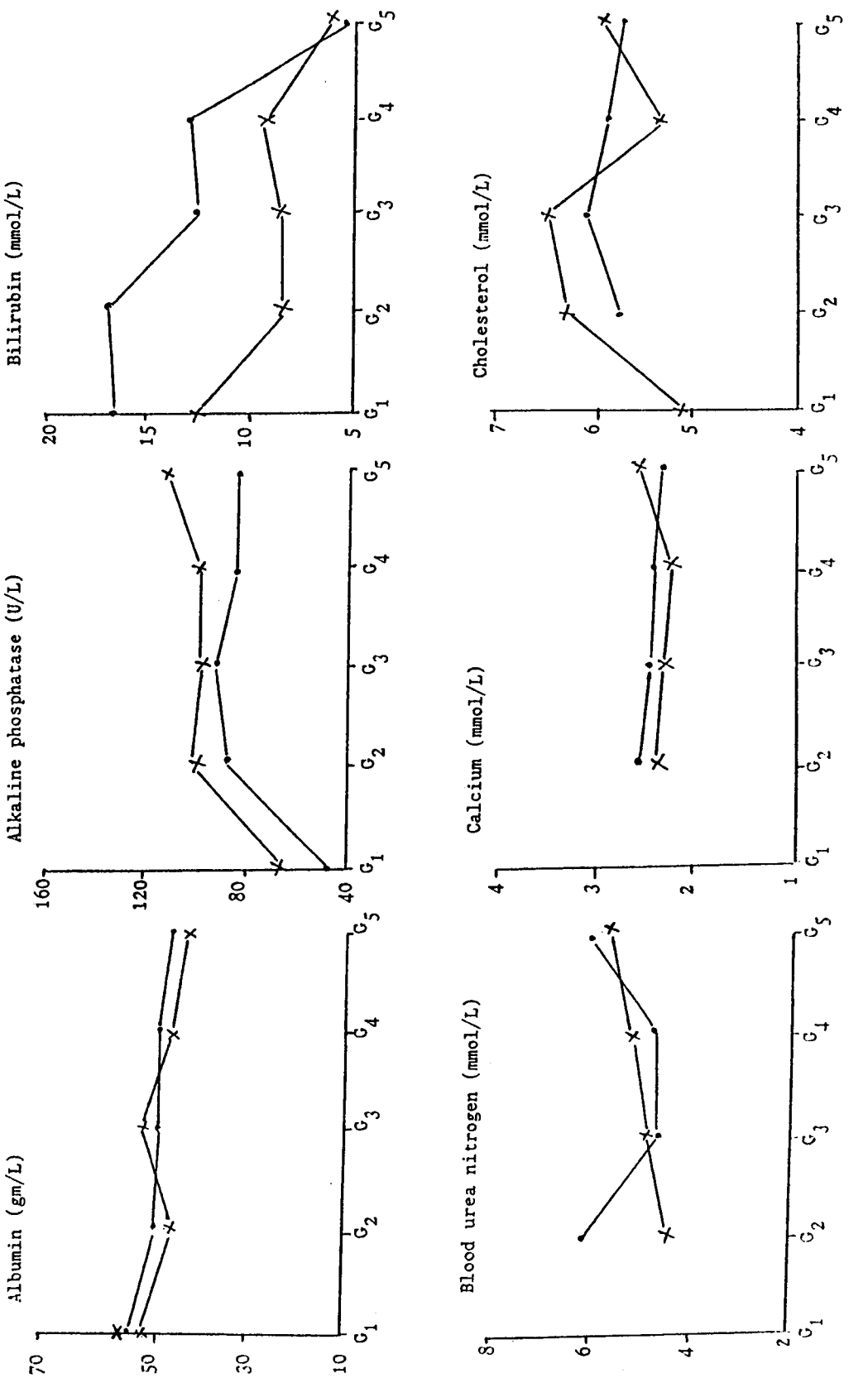

Figure 1. Serum biochemical substances of subjects
·___·· Males x____x Females

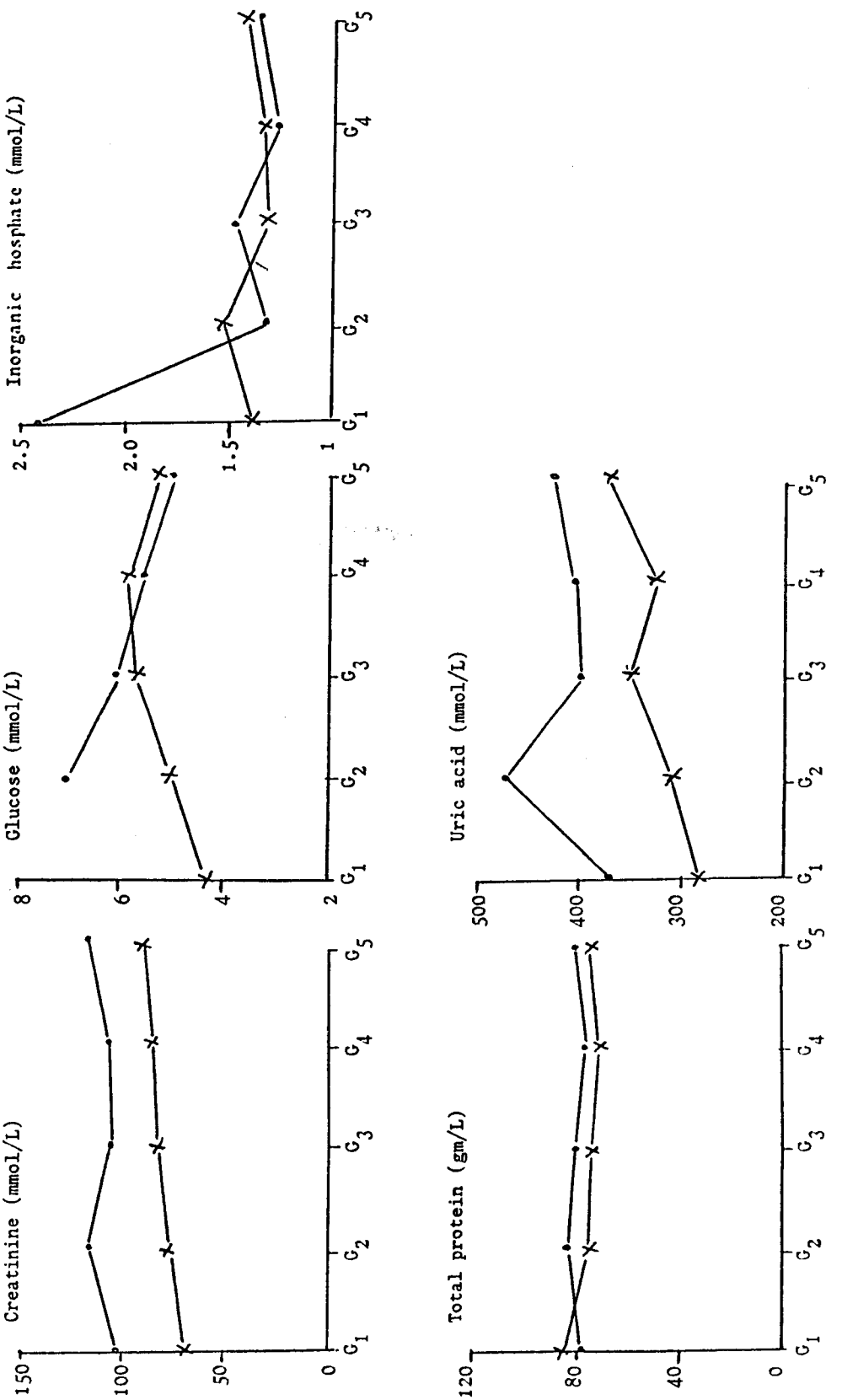

Figure 1. (continued): Serum biochemical substances of subjects
. Males x Females

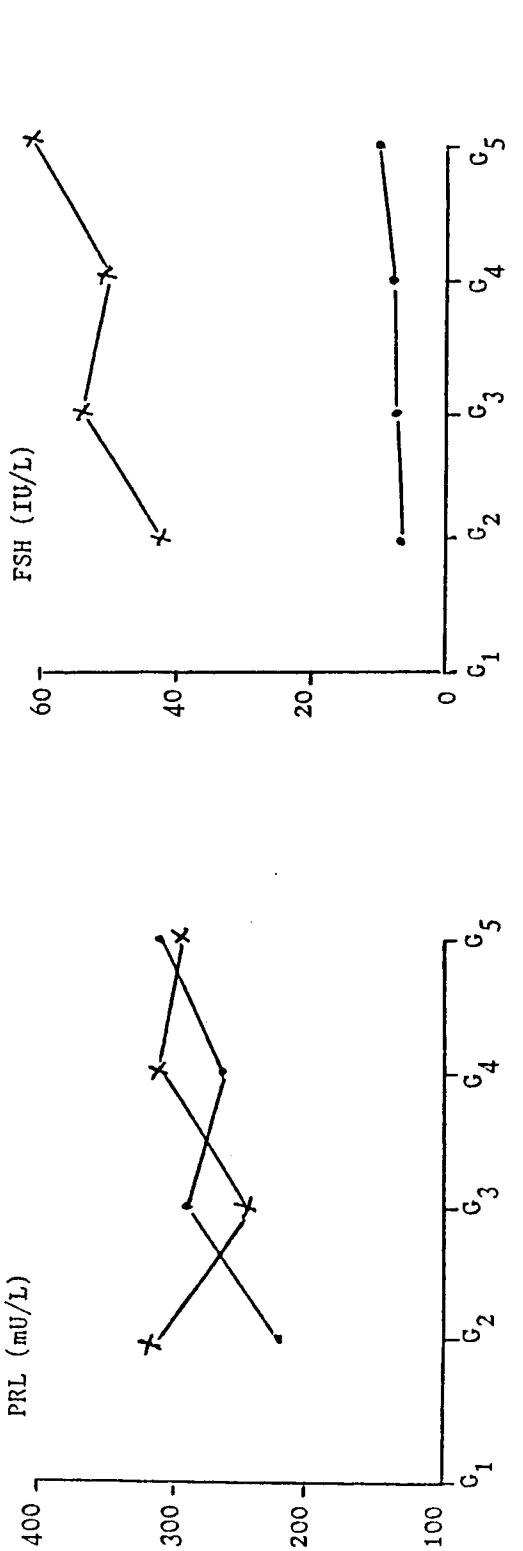

Figure 2. Serum hormonal levels of subjects.
. Males x Females

It was found that the levels of protein of the male and female elderly subjects were not different from those of reproductive age males and females.

Alkaline phosphatase was apparently higher in females than males in both the reproductive age and elderly groups.

The level of total bilirubin decreased with advancing age. Reproductive age males and females showed levels higher than those in the elderly group and males showed higher levels than females.

Elderly male and female subjects between the age of 80 and 89 years showed no difference in BUN levels, but among those 50-59 years, levels were higher in males than females.

Elderly subjects showed no difference in calcium levels. Also there was no difference between females of reproductive age and elderly subjects.

Reproductive age males and females showed no difference in cholesterol levels, while the elderly subjects showed higher levels. Females aged 50-69 years had higher cholesterol levels than males; decreasing levels were observed in those aged 70-89 years.

Both reproductive age and elderly males had higher creatinine levels than females. The creatinine levels of both groups showed no difference, but there was a tendency towards an increase in females.

Glucose levels in elderly females were higher than reproductive age females; males aged 50-59 years had higher glucose levels than females of the same age. Males and females aged 66-89 years showed no difference in glucose levels.

Reproductive age males had higher inorganic phosphate levels than females in the same group, but there was no difference in the levels of either males or females in the elderly subjects.

Uric acid in reproductive age males and those in the elderly group showed higher levels than females of equivalent age.

Hormonal levels

The hormonal levels of reproductive age subjects were not determined since there were insufficient specimens for the purpose. Therefore, the changes in hormonal levels were compared among the elderly group only.

It was found that the levels of PRL (between 200 and 300 mU/L) showed no difference in the elderly subjects.

The levels of FSH and LH in females was higher than in males. FSH of elderly females showed an increase from 40 to 60 IU/L when compared with the LH level, which was fairly constant at 30 IU/L. In elderly males, the LH level was also fairly constant at about 10 IU/L.

The testosterone level of elderly males at the age of 89 years had decreased (14 nmol/L). Approximately one fifth of the elderly males showed an estradiol level similar to that observed in the female follicular phase as previously described.[10] However, in most of the elderly females, it was undetectable.

Discussion

Furton and Burke[11] found that there was no difference in the albumin level of subjects between the ages of 23 and 82 years. They explained that hypoalbuminemia in elderly subjects was due to disease. Our findings showed that the level of albumin had a tendency to decrease, which is similar to the findings of Keating[8] and Cooper et al.[12]

Our study showed that the level of enzyme alkaline phosphatase increased with age, a finding similar to those reported by Robert[4] and Macus.[7]

A decreased level of calcium was found in females by Robert[4] and Yendt et al.[9] while we found no change. Our finding is similar to the reports of Lingarde[13] and Roof.[14] Yendt et al.[9] explained that the decrease was due to a decrease in protein-bound calcium. In addition, the different findings may be due to the different methods used for the determination. Apparently, there are four methods used for the determination of calcium, namely: o-cresolphthalein complexone, flame photometry, atomic absorption and titration technique. Each method has its own advantage and disadvandtage. In order to use the calcium level for biochemical interpretation, the determination of ionized calcium might be more useful than the level of total serum calcium.

The glucose level of elderly subjects in our study was similar to that of Fraser.[9] In addition, we found that elderly females had higher levels of glucose than reproductive age females. The imbalance in dietary intake of elderly subjects may result in the pancreas secreting insufficient insulin to draw glucose into the cells, which cause an increase in blood glucose.[15]

Morgan[1] found the serum inorganic phosphate level to be high in post-menopausal women, whereas Marcus[7] showed that the mean value of serum inorganic phosphate decreased with age, but he did not specify the age. Yendt et al.[9] reported that the phosphorus level decreased after the age of 65 years. However, Robert[4] and Allardt[6] found that there was no change in inorganic phosphate between the ages of 34 and 80 years. Our findings

indicate that elderly males and females showed lower phosphate levels than people of reproductive age.

Our finding indicates that the level of uric acid apparently increased with age and was more pronounced in males. This is caused when androgens in males stimulate the activity of the enzyme xanthine oxidase, which changes purine to uric acid. In addition, we found that there was a trend towards high uric acid levels in elderly females. This may be due to the decrease of estrogen in elderly females.

Elderly females showed a level of serum prolactin similar to the level found in the follicular phase of reproductive age women.[10]

FSH and LH levels were high in elderly females. The FSH level showed a higher level than LH because the normal production rate of these hormones is similar but the metabolic clearance rate of LH is twice as higher as that of FSH. The FSH half life is 3 hours while the LH is only 20 minutes.[13] Therefore, the level of FSH in the circulation was higher than LH. Our findings showed that both hormones levels were higher than those of people of reproductive age, as proviously described,[10] and also elderly females had higher levels than males.

The level of FSH and LH in males was rather constant at ages 50-79 years. Small changes were found at age 89 years.

The level of testosterone in males aged 50-79 years was about 17 IU/L; it decreased at age 89. The decrease in the testosterone level corresponded with a higher LH level.

Most of the estradiol level in elderly females could not be detected. The rate of estradiol synthesis decreased 93% and estrone decreased 25% in menopausal women, but the metabolic clearance rates of these two hormones are similar. Therefore, because estrone in circulation is higher than estradiol.[15] The determination of estrone in the circulation of elderly subjects would be useful for the study of hormonal changes in elderly people.

Most men show a higher level of estradiol than women. This is due to peripheral aromatization of androstenedione from the adrenal glands to estrogens.[17]

It may be concluded that the levels of albumin, alkaline phosphatase, total bilirubin, cholesterol, creatinine, glucose, inorganic phosphate and uric acid changed in elderly subjects. The results indicate that it is necessary to set reference values for biochemical substances in elderly Thai subjects, especially those between the ages of 70 and 89 years. In order to establish reference values for this age group, more subjects should be included in a similar study.

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