Acta Med. Okayama, 2018
Vol. 72, No. 5, pp. 447–456

Acta Medica Okayama
http://escholarship.lib.okayama-u.ac.jp/amo/

Original Article

Clinical Characteristics of Febrile Outpatients: Possible Involvement of Thyroid Dysfunction in Febrile Tachycardia

Kosuke Oka, Yoshihisa Hanayama, Asuka Sato, Daisuke Omura, Miho Yasuda, Ko Hasegawa, Mikako Obika, and Fumio Otsuka*

Department of General Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama 700-8558, Japan

We retrospectively analyzed the cases of 148 febrile patients whose body temperature (BT) was ≥37.5°C at our hospital. We categorized them into seven groups; those with bacterial and viral infection, nonspecific inflammation, neoplasm, connective tissue disease (CTD), drug-induced disease, and unidentified causes. Our analysis revealed that the patient's BT at the 1st visit (BT-1st visit) and highest BT during the febrile period (BT-max) differed significantly among all categories except neoplasm. The greatest difference between BT-1st visit and BT-max was highest in the CTD group (1.5°C). Positive correlations of heart rate and C-reactive protein (CRP) level with BT-max and a negative correlation between serum sodium level with BT-max were uncovered. The serum thyroid-stimulating hormone (TSH) level and the ratio of TSH/free thyroxine were negatively correlated with BT-max, especially in the viral infection group, suggesting the existence of occult thyrotoxicosis in accord with a febrile condition, possibly leading to febrile tachycardia. A febrile gap between BT-1st visit and BT-max (except in the neoplasm group) was shown, in which BT-max was correlated with thyroid function. Clinicians should recognize the fluctuation of BT when diagnosing febrile patients, and tachycardia in such febrile patients may be, at least in part, associated with subclinical thyroid dysfunction.

Key words: body temperature, C-reactive protein, fever of unknown origin, tachycardia, thyroid dysfunction

The diagnosis of the etiology of a patient's fever of unknown origin (FUO) is often challenging for general practice physicians, and there are sometimes very limited findings directly related to the causal disease(s) of a fever. In an outpatient unit, it can be very difficult to establish a final diagnosis and initiate appropriate treatment within the short period of a patient's visit.

Petersdorf and Beeson first proposed the classical definition of FUO in 1961 [1]. Their criteria included prolonged febrile illness of ≥3 weeks in duration with a fever >38.3°C and the cause being uncertain after 1 week of hospitalized investigation [1]. Durack and Street redefined FUO in 1991 to include, in addition to classical FUO, nosocomial, neutropenic and HIV-associated FUOs [2]. The original definition of classical FUO was modified to include fever with a cause that remains uncertain after a ≥3-day hospitalization or three hospital visits [2].

Since then, studies on FUO have been carried out worldwide [3-7], and several FUO studies have been conducted in Japan [8-13]. The latter studies investigated the reduced tendency of infectious disease [14] and the influence of various diagnostic methods [9] on the diagnosis of FUOs, including methods using fluo-

Received February 26, 2018; accepted May 8, 2018.
*Corresponding author. Phone: +81-86-235-7342; Fax: +81-86-235-7345
E-mail: fumiotsu@md.okayama-u.ac.jp (F. Otsuka)

Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

rodeoxyglucose-positron emission tomography (FDG-PET) [10] and procalcitonin [15]. In 2013, Naito *et al.* reported the results of the first nationwide survey on FUOs in Japan that examined the usefulness of inflammatory markers such as the white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), serum level of C-reactive protein (CRP), and serum level of procalcitonin for the diagnosis of FUO [11, 13].

Since the criteria for classical FUO are strict, recent studies have targeted a much wider spectrum of febrile patients [12, 14]. A study by Goto *et al.* dealt with not only classical FUO but also all febrile diseases with axillary temperatures above 37°C, and their analysis showed that the inclusion of a wider spectrum of febrile diseases is necessary for patients with a prolonged fever [16]. We also analyzed hospitalized febrile patients with axillary temperatures above 37.5°C in our department, and we reported that disease categorization is useful for the diagnosis of febrile etiology [17].

Although there have been various reports on fever as described above, the optimal management of a patient with an FUO remains difficult and necessitates an individual evaluation for each patient and an experienced physician [18]. The fundamental steps of taking a medical history and physical examination are still important [19]. In this study, we analyzed various clinical data of febrile outpatients with a focus on changes in body temperature (BT) and clinical and biochemical parameters.

Patients and Methods

Patients. We retrospectively analyzed the medical records of 148 febrile patients who visited the Department of General Medicine, Okayama University Hospital during the period from January 2012 to December 2012. The cases of patients with an axillary body temperature ≥37.5°C at their first visit (BT-1st visit) and those with a highest axillary body temperature >37.5°C during the febrile period (BT-max) were included. The patients were 75 males and 73 females with a mean age of 42.4 years (range 3-90 years). The study protocol (#K1506-014) was approved by the Institutional Review Board (IRB) of the Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences.

Laboratory examination. Blood cell counts, ESR, serum level of CRP, serum levels of electrolytes including sodium, and the levels of total cholesterol (T.Cho), blood sugar (BS), thyroid-stimulating hormone (TSH), and free thyroxine (FT4) were determined by an auto-analyzer system in the Central Laboratory of Okayama University Hospital. Serum CRP levels were determined by a latex-agglutination method using latex particles conjugated with anti-CRP antiserum, and the normal range was <0.3 mg/dl. The levels of serum TSH and FT4 were determined by an electrochemiluminescence immunoassay, and we selected the results regarding thyroid functions at the first or second visit for fever for the present analysis.

Statistical analysis. Results are shown as the mean ± SEM of the data. The data were subjected to Kruskal-Wallis and Mann-Whitney *U*-tests to determine significant differences between the groups. If differences were detected by the Kruskal-Wallis test, the Steel-Dwass *post-hoc* test was used to determine which means differed. The data were also analyzed by a linear regression analysis and Spearman's rank correlation coefficients to determine inter-relationships between parameters. *P*-values <0.05 were accepted as significant. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R commander (2.3-0) designed to add statistical functions frequently used in biostatistics [20].

Results

Profiling of febrile outpatients. The distribution of the patients' ages is shown in Fig. 1A. Among the patients (aged 3-90 years), a large proportion (58.1%) was relatively young (20-49 years old). As noted above, the gender distribution was 75 males (50.7%) and 73 females (49.3%). We categorized the patients into the following seven groups based on our previous study [17] (Fig. 1B): those whose fever was attributed to (1) a bacterial infection (Bacterial), (2) a viral infection (Viral), (3) nonspecific inflammation (NSI), (4) a neoplasm (Neoplasm), (5) connective tissue disease (CTD), (6) drug-induced disease (Drug), and (7) Unidentified.

The numbers and proportions of patients were Bacterial (n=32, 21.6%), Viral (n=49, 33.1%), NSI (n=14, 9.5%), Neoplasm (n=5, 3.4%), CTD (n=6, 4.05%), Drug (n=6, 4.05%), and Unidentified (n=36, 24.3%). The majority of the diseases was infectious dis-

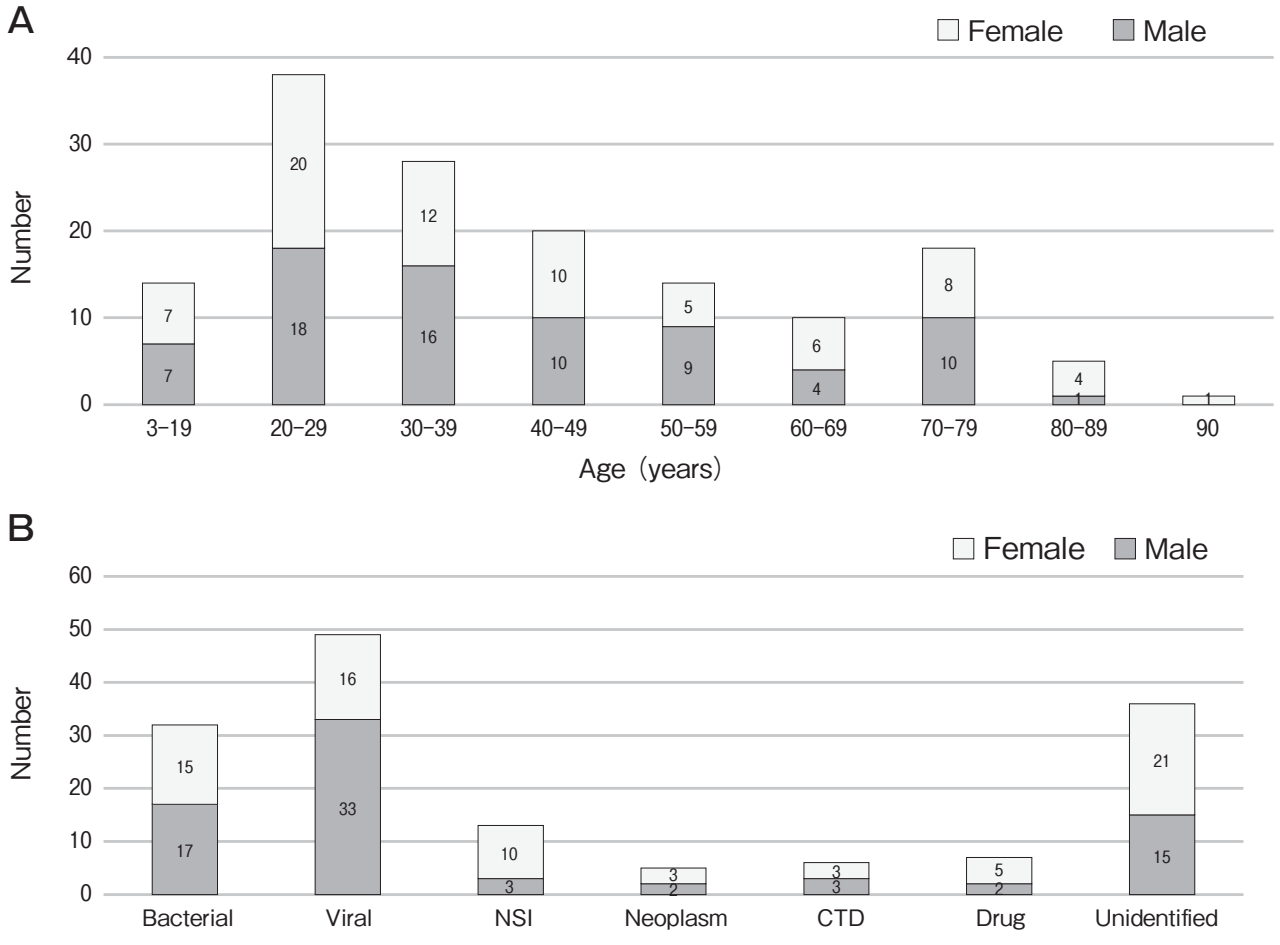

Fig. 1 Characteristics of febrile patients. **A**, Age distribution of the patients; **B**, Numbers and gender ratios in the categorized diseases. All febrile patients were classified into 7 groups: bacterial infection (Bacterial), viral infection (Viral), nonspecific inflammation (NSI), connective tissue disease (CTD), Neoplasm, drug-induced disease (Drug) and Unidentified cases. The female/male ratios are shown below.

eases, including Bacterial and Viral diseases, which together accounted for 54.7% of the cases. The female-to-male ratio was high in the NSI (3.3) and Drug groups (2.5), and the male-to-female ratio was high in the Viral group (2.1).

Febrile characteristics in each disease category. The data regarding the patients' age, duration of fever, and body temperature in the 7 groups are summarized in Fig. 2. The mean ages of the patients in the Neoplasm and CTD groups (>60 years) were significantly higher compared to the Viral group (<35 years) (Fig. 2A). The average fever durations were significantly different between the Viral and Unidentified groups (Fig. 2B). The febrile period was longest in the Unidentified group (>200 days) and shortest in the Viral group (8 days) and Drug group (<7 days). The patients in the CTD and Neoplasm groups had relatively long febrile durations (30-50 days). As shown in Fig. 2C, between-group differences in BT-1st visit and BT-max were revealed, with BT-max being significantly higher than BT-1st visit in all groups except the Neoplasm group.

Correlations between BT and clinical parameters. Based on the results shown in Fig. 2C, we focused on the relationships between BT-max and various parameters. Fig. 3 illustrates the relationships between BT-max and the clinical parameters of systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR) for the 134 patients in whom the HR was weakly but significantly correlated with BT-max ($r = 0.232$, $p < 0.01$). SBP and DBP were not significantly correlated with BT-max.

Correlations between BT and laboratory data.

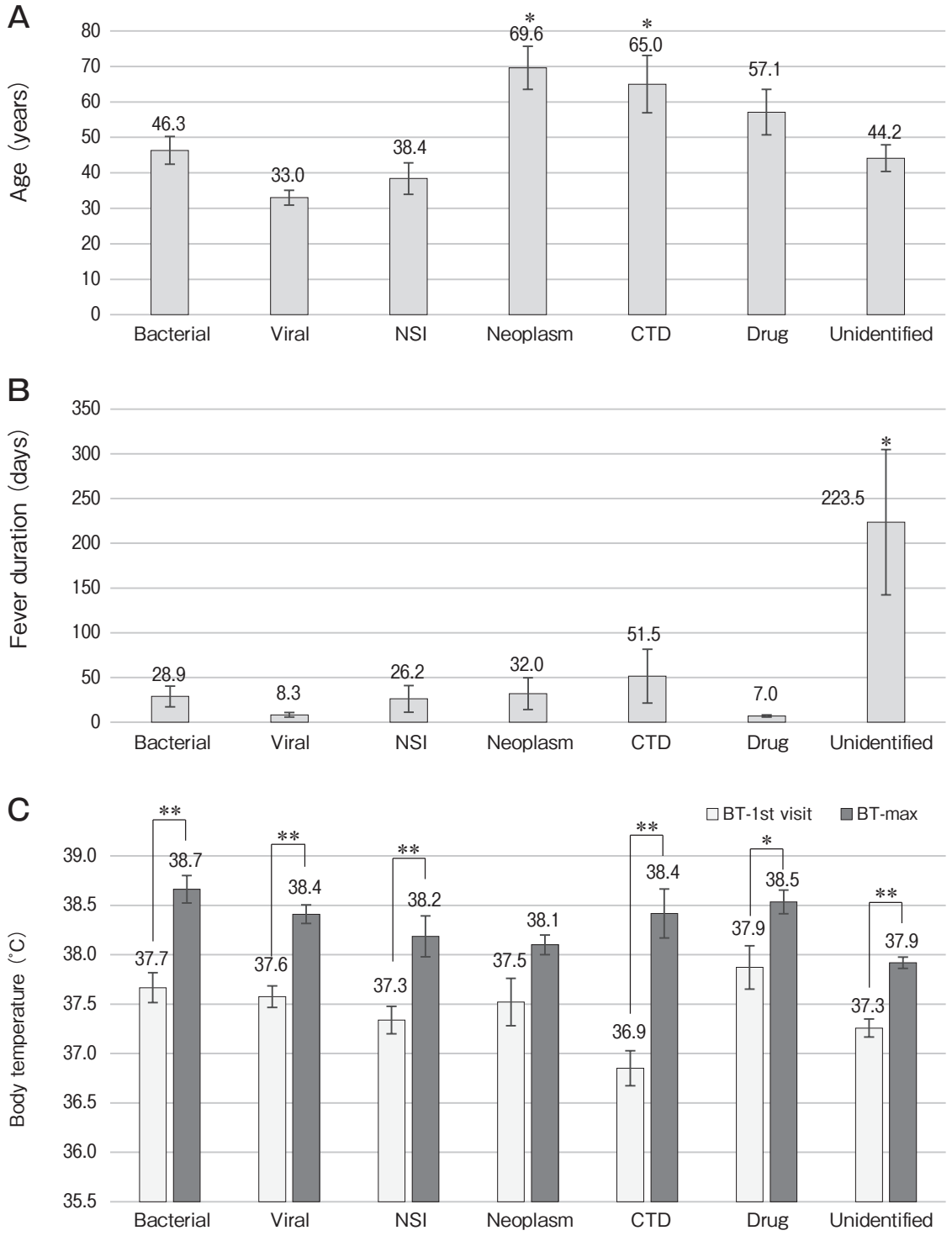

Fig. 2 Body temperature and fever duration. **A**, Mean ages in the categorized febrile groups (n = 148); **B**, Duration of fever before 1st visit (n = 148); **C**, Differences in body temperature at the 1st visit (BT-1st visit) and highest body temperature during the fever (BT-max) (n = 148). The results in each panel are shown as means ± SEM of data. Data were analyzed by the Kruskal-Wallis test (**A**, **B**) or by the Mann-Whitney *U* test for each group (**C**), and when a significant effect was observed, subsequent comparisons of group means were conducted. $^{*}P < 0.05$ vs. Viral group (**A**, **B**); and $^{*}P < 0.05$ and $^{**}P < 0.01$ between the indicated groups (**C**).

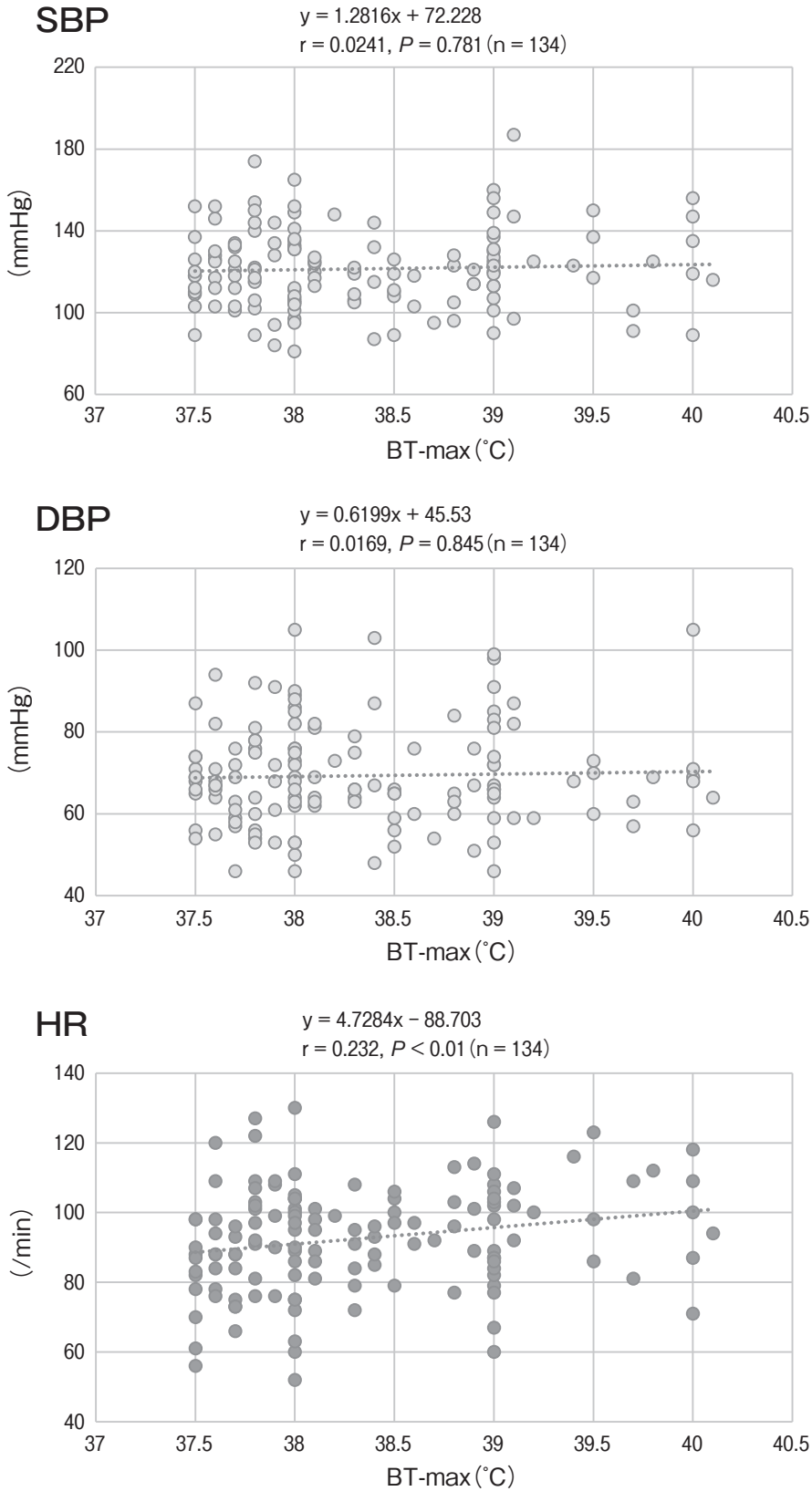

Fig. 3 Relationships between highest body temperature (BT-max) and clinical parameters. Correlations between body temperature and clinical parameters (SBP, DBP, and HR) were statistically analyzed by linear regression analysis.

Fig. 4 depicts the correlations of BT-max with major inflammatory markers (WBC, ESR, and CRP) and metabolic markers (sodium, T.Cho, and BS). The patients' CRP level was positively correlated with BT-max ($r = 0.306$, $p < 0.01$), and the sodium level was inversely correlated with BT-max ($r = -0.242$, $p < 0.01$). The levels of WBC, ESR, T.Cho, and BS were not significantly correlated with BT-max.

Correlations between BT and thyroid functions. The relationships between BT-max and thyroid functions including serum levels of TSH and FT4 and ratio of TSH/FT4 are shown in Fig. 5. TSH was measured in 64 febrile patients, and FT4 was also measured in 61 febrile patients including one patient with subacute thyroiditis, one patient with silent thyroiditis, and three patients with a past history of Graves' disease. We observed that the patients' TSH level was negatively correlated with BT-max ($r = -0.515$, $p < 0.01$) and that the FT4 level was positively correlated with BT-max ($r = 0.377$, $p < 0.01$). In addition, the ratio of TSH/FT4 was negatively correlated with BT-max ($r = -0.547$, $p < 0.01$). The correlations between BT-max and TSH/FT4 ratio for each disease category were as follows: Bacterial: $r = -0.374$, $p = 0.208$ (13 cases); Viral: $r = -0.672$, $p = 0.0473$ (9 cases); CTD: $r = -0.8$, $p = 0.333$ (4 cases); Drug: $r = -0.1$, $p = 0.95$ (5 cases); NSI: $r = -0.699$, $p = 0.0538$ (8 cases); and Unidentified: $r = -0.37$, $p = 0.0898$ (22 cases).

Four patients were observed to have abnormally high levels of serum FT4 (Fig. 5). One was a patient with bacterial prostatitis accompanying silent thyroiditis (in the Bacterial group), whose serum FT4 level was 3.95 ng/dl and BT-max was 40°C. Another two patients were subacute thyroiditis (in the NSI group) and histiocytic necrotizing lymphadenitis accompanying Graves' disease (in the NSI group), whose serum FT4 levels were 2.72 and 2.93 ng/dl and BT-max were 39°C and 38.9°C, respectively. The other patient's case was thyrotoxicosis triggered by allergic reaction (in the Drug group); hisserum FT4 level was 5.39 ng/dl and the BT-max was 38.3°C.

Discussion

We analyzed clinical data including the BT, SBP, DBP, HR and laboratory data for 148 febrile outpatients who visited our Department of General Medicine during a 1-year period. We recently showed the usefulness of the categorization of febrile patients into seven groups [17]. Compared to the data for our inpatients, among the present study's outpatients the proportion of patients with a non-bacterial/viral infection was higher and the proportion of patients with a neoplasm or CTD was lower: bacterial infection (21.6% in the present study vs. 23.6% in our inpatient data), non-bacterial infection (33.1% vs. 17.8%), NSI (9.5% vs. 14.9%), Neoplasm (3.4% vs. 6.9%), CTD (4.05% vs. 12.0%), Drug (4.05% vs. 5.7%), and Unidentified (24.3% vs. 19.0%). Patients with infectious diseases including Bacterial (21.6%) and Viral (33.1%) diseases accounted for approximately half of all patients, suggesting that many of the common infectious diseases (*e.g.*, upper respiratory tract inflammation and infectious gastroenteritis) were incorporated in this series of febrile outpatients.

Regarding the patients' profile, the average ages of the patients in the Neoplasm and CTD groups were significantly higher than the average age in the Viral group. The febrile period in the Viral group was significantly shorter than that in the Unidentified group. The patients in the CTD and Neoplasm groups had a relatively long febrile period (> 30 days), but this was statistically insignificant.

In the present study of outpatients, the first important finding was the difference in BT as shown between BT-1st visit and BT-max. The difference in BT was remarkable in the CTD group, with BT-max at > 1.5°C higher than the BT-1st visit values. Although there has been no clear report on daily BT changes in febrile patients, it was noted that the BT of febrile patients such as patients with familial Mediterranean fever tends to fluctuate daily [21], and the febrile changes between visits may also be influenced by antipyretics taken before visits. Considering that in our series key laboratory data were more strongly correlated with BT-max than with BT-1st visit (data not shown), clinicians should inquire in detail about a patient's body temperature even if the patient does not have a fever at the time of his/her visit, particularly for outpatients.

Among the laboratory parameters we examined on the basis of BT-max, the serum level of CRP was weakly but significantly correlated with BT-max, whereas the serum sodium level was negatively correlated with BT-max. The correlations of BT with other biomarkers or clinical findings examined herein were not statistically significant. The results regarding the correlation

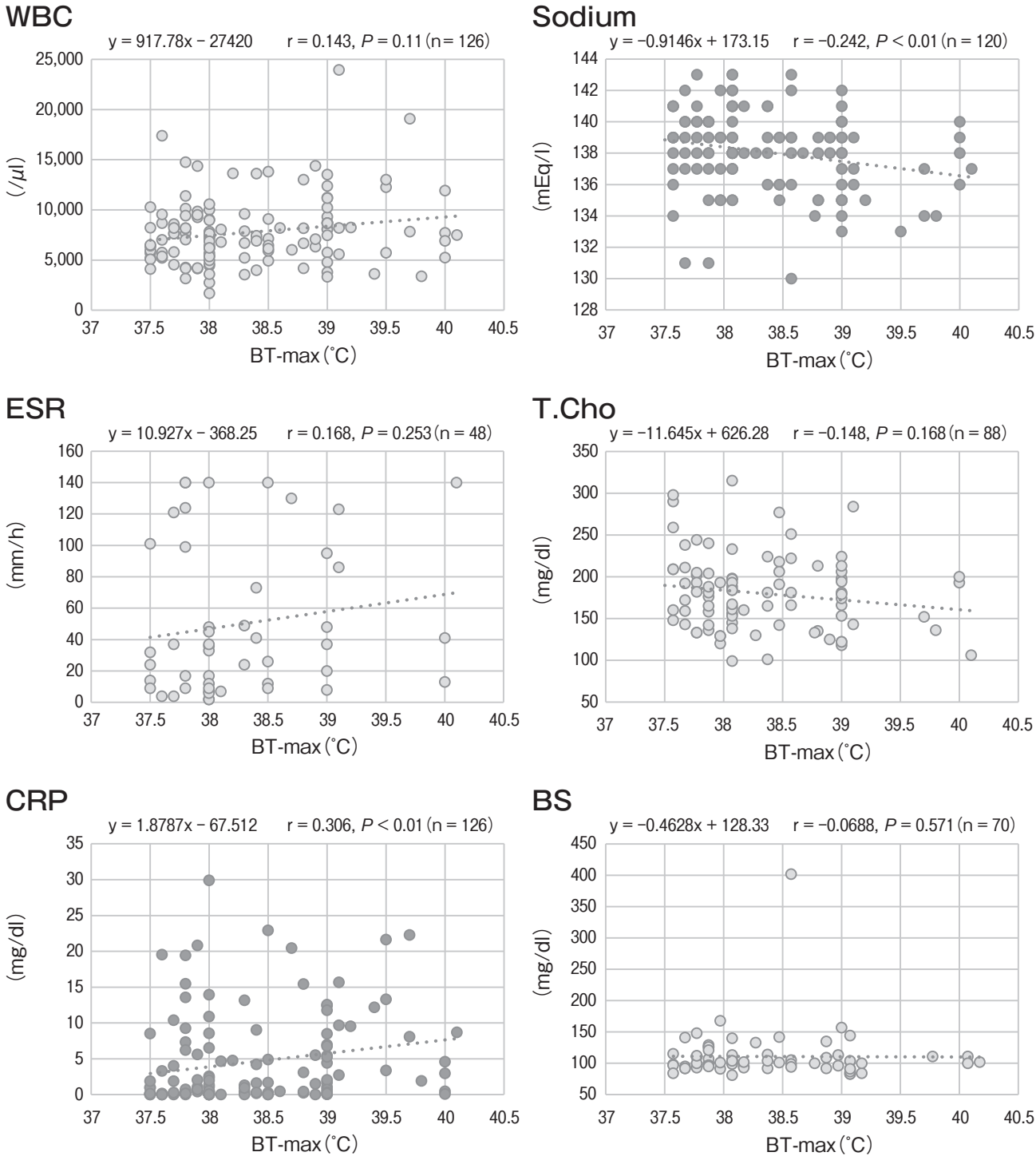

Fig. 4 Relationships between highest body temperature (BT-max) and various biomarkers. Correlations between body temperature and biomarkers (WBC, ESR, CRP, Sodium, T-Cho, and BS) were statistically analyzed by linear regression analysis.

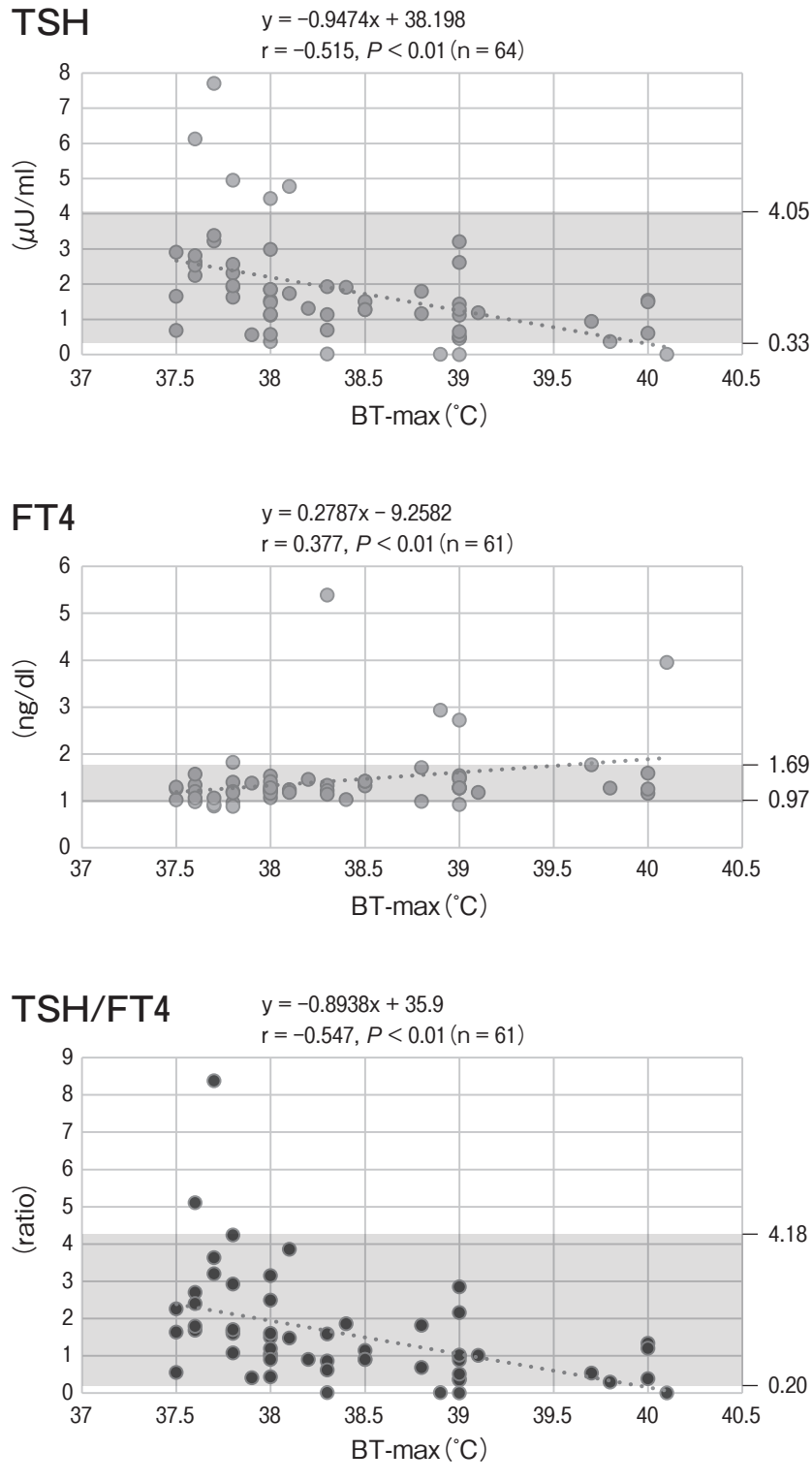

Fig. 5 Relationships between highest body temperature (BT-max) and thyroid function. Correlations between body temperature and thyroid function (TSH, FT4, and TSH/FT4) were statistically analyzed by linear regression analysis. The areas of shadow indicate the normal ranges of thyroid functions (TSH: 0.33–4.05 μU/mL, FT4: 0.97–1.69 ng/dL, and TSH/FT4: 0.2–4.18).

between CRP and BT-max in this study and in our previous study of inpatients [17] showed similar tendencies, suggesting that the degree of inflammation shown by the CRP level reflects the patient's febrile condition.

Regarding the changes in serum sodium levels, an inverse relationship between sodium and febrile condition was shown [22], implying that the BT was associated with lower sodium conditions, possibly due to susceptibility to SIADH (syndrome of inappropriate secretion of antidiuretic hormone) induced by febrile stress. The involvement of prostaglandin E2, which acts on the hypothalamus to raise the BT and affects sodium reabsorption from the proximal tubules of the kidneys, might be associated with the phenomenon of febrile hyponatremia [23].

A second major finding revealed by our present investigation was the involvement of thyroid dysfunction shown by TSH/FT4 ratios in the febrile conditions of these outpatients. In this patient series, the TSH/FT4 ratio was significantly correlated with BT-max. Thus far, a correlation between fever and thyroid function has not been reported, to our knowledge. Considering a report showing that a subcutaneous administration of interleukin-6 (IL-6) can decrease TSH and increase FT4 [24], a febrile condition may stimulate the production of IL-6, leading to a relatively thyrotoxicotic condition in vivo.

Regarding the correlation between BT-max and HR, it is known that the heart rate is elevated in febrile patients because of sympathetic enhancement [25]. However, it is also known that some febrile patients exhibit relative bradycardia caused by drug-induced fever, tumor-induced fever, specific infectious diseases, or other conditions [26]. Some studies have shown that fever may directly influence sodium channels, causing tachyarrhythmia [27,28]. Various factors are thus speculated to be involved in febrile tachycardia, but the mechanism of febrile tachycardia has not been clarified. Thyrotoxicosis is often caused by stress conditions such as surgery and viral infection [29,30]. As shown by our present analyses, only the Viral group showed a significant correlation between the BT-max and the TSH/FT4 ratio. Fever itself may be a stress condition and the cause of potential thyrotoxicosis, leading to tachycardia.

Considering that potential thyrotoxicosis accompanies a febrile condition, although a thyroid crisis is provoked by stress conditions such as infection and surgery, fever itself may be the cause of the thyroid crisis [31,32]. When clinicians encounter febrile patients, they should exclude the possibility of thyroid crisis since fever and tachycardia are significant symptoms of thyroid crisis, and it is also important to evaluate thyroid findings for undiagnosed febrile patients. Since potential thyrotoxicosis may be the cause of unpleasant subjective symptoms of febrile patients such as palpitation, fatigue and irritability, treatment for occult thyrotoxicosis may be effective for improving unpleasant symptoms.

In conclusion, our analyses revealed that a patient's body temperature at the first hospital visit for fever (BT-1st visit) and patients' highest body temperature during the febrile period (BT-max) are significantly different, and that BT-max is significantly correlated with key parameters including thyroid function. When clinicians encounter outpatients complaining of fever, a detailed inquiry about the patients' body temperature should be conducted, including an examination of body temperature fluctuation, since the BT-max in the febrile period may predict the patient's condition more accurately than the BT-1st visit. Since the number of cases and detailed information regarding thyroid diseases in the present series are limited, a multicenter study with an endocrinological investigation is necessary. Our findings revealed that thyroid dysfunction occurs in febrile patients and that tachycardia in febrile patients may be, at least in part, associated with subclinical thyroid dysfunction.

Acknowledgments. This study was supported partly by Grants-in-Aid for Scientific Research (Nos. 25670359 and 16K09257). We thank all of the physicians and medical staff who contribute to the patient care in the Department of General Medicine of Okayama University Hospital.

References

1. Petersdorf RG and Beeson PB: Fever of unexplained origin: Report on 100 cases. Medicine (Baltimore) (1961) 40: 1–30.
2. Durack DT and Street AC: Fever of unknown origin–reexamined and redefined. Curr Clin Top Infect Dis (1991) 11: 35–51.
3. Jacoby GA and Swartz MN: Fever of undetermined origin. N Engl J Med (1973) 289: 1407–1410.
4. Esposito AL and Gleckman RA: A diagnostic approach to the adult with fever of unknown origin. Arch Intern Med (1979) 139: 575–579.
5. Arnow PM and Flaherty JP: Fever of unknown origin. Lancet (1997) 350: 575–580.
6. Cunha BA: Fever of unknown origin. Infect Dis Clin North Am (1996) 10: 111–127.
7. Gaeta GB, Fusco FM and Nardiello S: Fever of unknown origin: A

systematic review of the literature for 1995–2004. Nucl Med Commun (2006) 27: 205–211.
8. Iikuni Y, Okada J, Kondo H and Kashiwazaki S: Current fever of unknown origin 1982–1992. Intern Med (1994) 33: 67–73.
9. Shoji S, Imamura A, Imai Y, Igarashi A, Yazawa M, Hirahara K, Kagoshima M, Ono M, Nakajima K and Iguchi K: Fever of unknown origin: A review of 80 patients from the shin'etsu area of japan from 1986–1992. Intern Med (1994) 33: 74–76.
10. Kubota K, Nakamoto Y, Tamaki N, Kanegae K, Fukuda H, Kaneda T, Kitajima K, Tateishi U, Morooka M, Ito K, Minamimoto R and Murakami K: Fdg-pet for the diagnosis of fever of unknown origin: A japanese multi-center study. Ann Nucl Med (2011) 25: 355–364.
11. Naito T, Mizooka M, Mitsumoto F, Kanazawa K, Torikai K, Ohno S, Morita H, Ukimura A, Mishima N, Otsuka F, Ohyama Y, Nara N, Murakami K, Mashiba K, Akazawa K, Yamamoto K, Senda S, Yamanouchi M, Tazuma S and Hayashi J: Diagnostic workup for fever of unknown origin: A multicenter collaborative retrospective study. BMJ Open (2013) 3: e003971.
12. Yamanouchi M, Uehara Y, Yokokawa H, Hosoda T, Watanabe Y, Shiga T, Inui A, Otsuki Y, Fujibayashi K, Isonuma H and Naito T: Analysis of 256 cases of classic fever of unknown origin. Intern Med (2014) 53: 2471–2475.
13. Naito T, Torikai K, Mizooka M, Mitsumoto F, Kanazawa K, Ohno S, Morita H, Ukimura A, Mishima N, Otsuka F, Ohyama Y, Nara N, Murakami K, Mashiba K, Akazawa K, Yamamoto K, Tanei M, Yamanouchi M, Senda S, Tazuma S and Hayashi J: Relationships between causes of fever of unknown origin and inflammatory markers: A multicenter collaborative retrospective study. Intern Med (2015) 54: 1989–1994.
14. Kasai K, Mori M, Hara R, Miyamae T, Imagawa T and Yokota S: National survey of childhood febrile illness cases with fever of unknown origin in japan. Pediatr Int (2011) 53: 421–425.
15. Hu L, Shi Q, Shi M, Liu R and Wang C: Diagnostic value of pct and crp for detecting serious bacterial infections in patients with fever of unknown origin: A systematic review and meta-analysis. Appl Immunohistochem Mol Morphol (2017) 25: e61–e69.
16. Goto M, Koyama H, Takahashi O and Fukui T: A retrospective review of 226 hospitalized patients with fever. Intern Med (2007) 46: 17–22.
17. Ryuko H and Otsuka F: A comprehensive analysis of 174 febrile patients admitted to okayama university hospital. Acta Med Okayama (2013) 67: 227–237.
18. Kaya A, Ergul N, Kaya SY, Kilic F, Yilmaz MH, Besirli K and Ozaras R: The management and the diagnosis of fever of unknown origin. Expert Rev Anti Infect Ther (2013) 11: 805–815.
19. Cunha BA, Lortholary O and Cunha CB: Fever of unknown origin: A clinical approach. Am J Med (2015) 128: 1138 e1131–1138 e1115.
20. Kanda Y: Investigation of the freely available easy-to-use software 'ezr' for medical statistics. Bone Marrow Transplant (2013) 48: 452–458.
21. Kunimatsu J, Maeda J, Watanabe R, Kato O, Kishida D, Yazaki M and Nakamura A: Fever of unknown origin in the outpatient setting: A retrospective analysis of 30 cases of familial mediterranean fever. Nihon Rinsho Meneki Gakkai Kaishi (2016) 39: 130–139.
22. Bucher C, Tapernoux D, Diethelm M, Buscher C, Noser A, Fehr T and Henz S: Influence of weather conditions, drugs and comorbidities on serum na and cl in 13000 hospital admissions: Evidence for a subpopulation susceptible for siadh. Clin Biochem (2014) 47: 618–624.
23. Norregaard R, Kwon TH and Frokiaer J: Physiology and pathophysiology of cyclooxygenase-2 and prostaglandin e2 in the kidney. Kidney Res Clin Pract (2015) 34: 194–200.
24. Torpy DJ, Tsigos C, Lotsikas AJ, Defensor R, Chrousos GP and Papanicolaou DA: Acute and delayed effects of a single-dose injection of interleukin-6 on thyroid function in healthy humans. Metabolism (1998) 47: 1289–1293.
25. Low DA, Keller DM, Wingo JE, Brothers RM and Crandall CG: Sympathetic nerve activity and whole body heat stress in humans. J Appl Physiol (1985) (2011) 111: 1329–1334.
26. Cunha BA: The diagnostic significance of relative bradycardia in infectious disease. Clin Microbiol Infect (2000) 6: 633–634.
27. Noris M, Carrillo A, Campuzano O, Santaella A, Brugada R, Garcia-Niebla J and Fiol M: Syncope and polymorphic ventricular tachycardia in the setting of a febrile illness. J Electrocardiol (2013) 46: 666–669.
28. Samani K, Wu G, Ai T, Shuraih M, Mathuria NS, Li Z, Sohma Y, Purevjav E, Xi Y, Towbin JA, Cheng J and Vatta M: A novel scn5a mutation v1340i in brugada syndrome augmenting arrhythmias during febrile illness. Heart Rhythm (2009) 6: 1318–1326.
29. So PC: Unmasking of thyrotoxicosis during anaesthesia. Hong Kong Med J (2001) 7: 311–314.
30. Alexander V, Kurien TT and Chattopadhyay A: An uncommon endocrine cause of pyrexia of unknown origin. J Assoc Physicians India (2009) 57: 527–528.
31. Akamizu T, Satoh T, Isozaki O, Suzuki A, Wakino S, Iburi T, Tsuboi K, Monden T, Kouki T, Otani H, Teramukai S, Uehara R, Nakamura Y, Nagai M, Mori M and Japan Thyroid A: Diagnostic criteria, clinical features, and incidence of thyroid storm based on nationwide surveys. Thyroid (2012) 22: 661–679.
32. Burch HB and Wartofsky L: Life-threatening thyrotoxicosis. Thyroid storm. Endocrinol Metab Clin North Am (1993) 22: 263–277.