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Significance of Rises in Urinary Bicarbonate Contents and pH Related with Increased Atmospheric Carbon Dioxide in Tokyo

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Tomoda, A., Kazuka, M., Yashima, K., Niiyama, K. and Muro, D. *Significance of Rises in Urinary Bicarbonate Contents and pH Related with Increased Atmospheric Carbon Dioxide in Tokyo.* Tohoku J. Exp. Med., 1997, **183** (1), 67-73 —— Atmospheric carbon dioxide concentration was measured at several locations in Tokyo, for two weeks, in December, 1995 and 1996, and was found to be increased up to 550 ppm, while it was shown by us to be 450 ppm in December, 1994. These results demonstrate that atmospheric carbon dioxide is steadily increasing at faster rates in Tokyo than we expect, though it has been considered that the atmospheric carbon dioxide is still as much as 350 ppm. Bicarbonate concentration and pH of urine of 13 medical students in Tokyo were also measured for the same period in December of 1995 and 1996, and were found to be significantly increased compared with the values that were reported in the past. Furthermore, urinary bicarbonate and pH were extensively increased, when 4 and 5 students made 3-hour car trip in two different cars with all windows closed, where carbon dioxide was increased up to about 5000 ppm within 1 hour. These results support our previous hypothesis that the increase of atmospheric carbon dioxide may be reflected by the increase of urinary bicarbonate and pH. Our results also suggest that the environmental situation is being seriously aggravated in Tokyo, year by year, in terms of atmospheric carbon dioxide. —— atmospheric carbon dioxide; urinary bicarbonate and pH

Atmospheric carbon dioxide has been increasing continuously and globally, due to annual increases in the consumption of fossil fuels (Chan 1990). In 1950, the concentration of carbon dioxide in the air was as low as 300 ppm (Berry and Colls 1990; Chan 1990). But, it was estimated to be 350 ppm in the remote global troposphere, from 1981 to 1984 (Conway et al. 1988). Such value seems to be considered to be maintained since then (Berry and Colls 1990; Chan 1990). The increase of atmospheric carbon dioxide is considered to cause warming of the earth and changes in global climate, but it remains unclear whether the increase in atmospheric carbon dioxide exerts some influence on the human body.

Pitts et al. (1949) reported that the amounts of urinary bicarbonate of normal

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adults are negligible and that the pH of urine is around 5.5. These values seems to have been considered as the standards for more than 40 years. In light of the recent increase of atmospheric carbon dioxide, it is conceivable that urinary bicarbonate and pH may be increased due to the following mechanism. Namely, the increase of the inhaled amount of carbon dioxide causes an increase of bicarbonate in blood through the action of erythrocyte carbonic anhydrase (Armstrong et al. 1966), resulting in the increased excretion of bicarbonate into urine (Pitts et al. 1949; Schwartz et al. 1959).

We previously reported that urinary bicarbonate and the pH of urine of adult Tokyo citizens was substantially higher compared with those of adult Kanazawa citizens, which might be attributed to the increased inhaled amounts of carbon dioxide in the air (Hamashima et al.1993). We further studied the concentration of atmospheric carbon dioxide, for 2 weeks, in December, 1994 and found that it was about 450 ppm in Tokyo, and about 350 ppm in Kanazawa city (Tomoda et al.1995). However, we found that the atmospheric carbon dioxide was about 550 ppm at several locations in Tokyo, in December, 1995. This fact prompted us to reinvestigate the urinary bicarbonate and pH in adult Tokyo citizens for 2 weeks in December, 1995 and 1996.

Materials and Method

Determination of atmospheric carbon dioxide. Concentrations of carbon dioxide in the air were determined outside and indoors at several locations in Tokyo by a portable CO_2 meter (Shibata Kagaku Co., Ltd., Tokyo). Measurements were made during the afternoon, from December 5th to 15th, 1995 and December 5th to 17th, 1996. The wind was minimal, it was fine, and outside temperature was from 4°C to 12°C for these periods, in Tokyo.

Collection of urine. After obtaining their informed consents, urine samples were collected from 13 students (13 men, aged 21 to 25 year of age) of Tokyo Medical College, December 5th to 15th, 1995, and from different 13 students (8 men and 5 women, aged 21 to 25 year of age), December 5th to 17th, 1996. Immediately after the excretion of urine into a 200 ml paper cup, urine was transferred via syringe into a 10 ml rubber-capped vacuum glass tube (Veno-ject; Terumo Co., Ltd., Tokyo). The values of pH, CO_2, and bicarbonate remained constant in a tube at room temperature for 24 hours as we demonstrated previously (Tomoda et al. 1995).

Determination of urinary bicarbonate, CO_2 and pH. Urine was collected from above-stated students at Tokyo Medical College, during the time period between 10 : 00 and 11 : 00 a.m. and between 4 : 00 and 5 : 00 p.m. (in December of 1995 and 1996).

Urinary bicarbonate, CO_2 and pH were analyzed by Hitachi 8800 type automatic blood gas analyzer (Hitachi Co., Ltd., Tokyo), just after collecting urine samples, as described previously (Tomoda et al. 1995).

Determination of urinary bicarbonate, CO_2 and pH after 3-hour trip by car with all windows closed. Five or four students stayed in different moving cars with all windows closed for 3-hour, on 9th, and 16th, December, 1996, respectively. During 3 hours trip, the concentration of carbon dioxide in the car was measured at constant intervals. Before and after the trip, urine was collected and was subjected to the analysis of urinary bicarbonate and pH.

Statistics. The mean pH and bicarbonate values, obtained under the different situations were compared by Student's *t*-test.

Results

The atmospheric carbon dioxide measured at various locations in Tokyo, in December, 1995 and 1996, was summarized in Table 1. For examples, the atmospheric carbon dioxide was 600 ppm at the campus of Tokyo Medical College, 1050 ppm at a cinema (indoor), 1800 ppm in a subway train; on December 6th, 1995. On December 9th, 1996, the atmospheric carbon dioxide was 600 ppm at Haneda airport (outdoor), 1400 ppm on a metropolitan highway, near Tsukishima, Tokyo (where traffic was extremely heavy).

Table 1. *Atmospheric carbon dioxide measured at several locations in Tokyo, in December, 1995 and 1996*

December 6, 1995	
Campus of Tokyo Medical College	600 ppm
Yasukuni Street, Shinjuku, Tokyo	550 ppm
A street in Kabukicho, Shinjuku	550 ppm
A subway station, Shinjuku	850 ppm
In a subway train	1800 ppm
In a cinema, Shinjuku	1050 ppm
December 9, 1996	
Haneda Airport (outdoors)	600 ppm
Metropolitan highway, Tokyo	
near Odaiba	550 ppm
near Ooi-minami	700 ppm
near Tsukishima	1400 ppm
inside the Iikura tunnel	1200 ppm
Campus of Tokyo Medical College	600 ppm
December 12, 1996	
Campus of Tokyo Medical College	600 ppm
Subway 1. (a station, crowded with many passengers)	3800 ppm
Subway 2. (a station, crowded with many passengers)	2000 ppm
Main street, Ginza, Tokyo	600 ppm

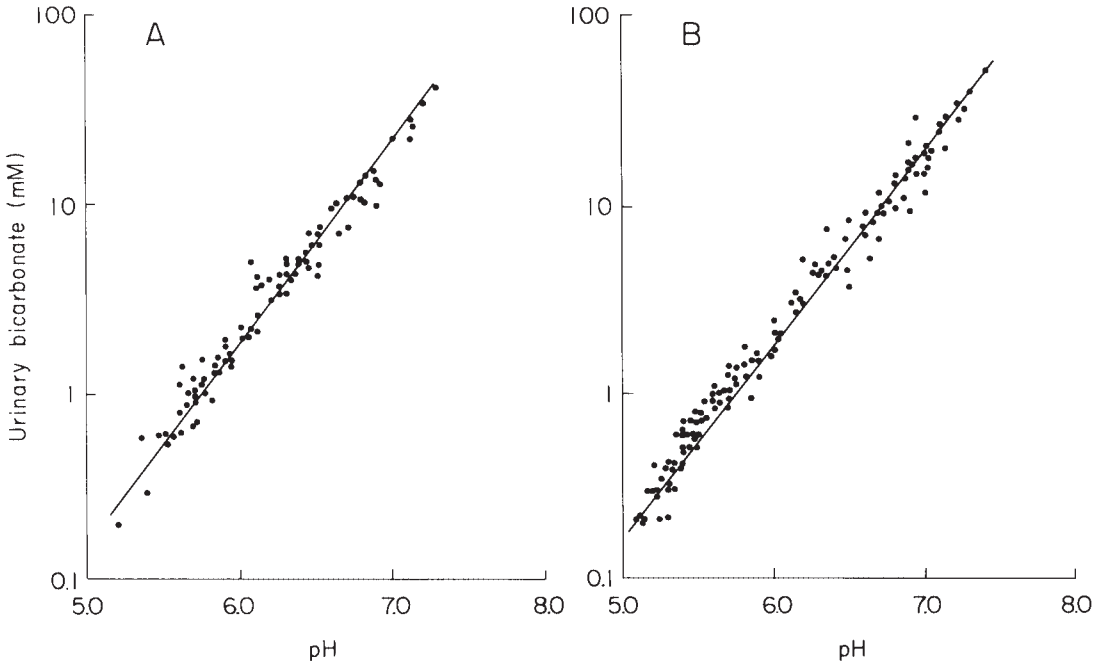

Fig. 1. Relationship between urinary bicarbonate and pH of the students. Urine samples were collected from healthy students (13 men) from December 6th to 15th, 1995 and from healthy students (8 men and 5 women) from December 6th to 17th, 1996, and the concentration of urinary bicarbonate and urinary pH were analyzed. The concentration of urinary bicarbonate was expressed logarithmically. (A) 1995 Data ($r=0.945$, $p<0.01$) (B) 1996 Data ($r=0.978$, $p<0.01$)

Fig. 1A shows the concentration of urinary bicarbonate of 88 specimens from 13 medical students (analyzed from December 5th to December 15th, 1995) as a function of urinary pH. Urinary bicarbonate concentrations were closely related with the pH of urine ($r=0.945$, $p<0.01$). The mean values of urinary bicarbonate and pH were 5.8 mM and 6.21, respectively. The highest values of urinary bicarbonate and pH of the urine of a student were 40.2 mM and 7.29, respectively, though the conditions of this student were normal when the urine was collected, and he did not drink a beverage containing carbonic acid before collecting urines.

Fig. 1B also shows the concentrations of urinary bicarbonate of 134 specimens of 8 male and 5 female medical students (whose urine was collected from December 5th to 17th, 1996) as a function of urinary pH ($r=0.978$, $p<0.01$). The mean values of urinary bicarbonate and pH were 6.3 mM and 6.00, respectively, similar to those obtained in 1995. The highest values of urinary bicarbonate and pH of the urine of a student were 50.6 mM and 7.42, respectively.

Since the increased atmospheric carbon dioxide seems to affect the excretion of bicarbonate into urine and urinary pH, we studied the changes in urinary bicarbonate and pH of students, who stayed in a compact car that was driven for 3 hours with its all the windows closed. Fig. 2 shows the changes in urinary bicarbonate of these students before and after the trip. After 3-hour trip, the urinary bicarbonate increased significantly in every student, being in good accor-

dance with the prominent increase of urinary pH. During 3-hour trip, carbon dioxide in a car with all windows closed increased from 550 ppm to 2000 ppm, within 30 minutes, reached about 5000 ppm within one hour, and then continued to be about 5000 ppm thereafter. The atmospheric carbon oxide was about 600 ppm at the campus of Tokyo Medical College, the starting and ending point, on these days.

Discussion

We studied the concentration of atmospheric carbon dioxide, in December, 1995 and 1996, and found that it increased up to about 550 ppm at the several locations of Tokyo (Table 1). On the metropolitan highway, where the traffic is very heavy, more than 600 ppm carbon dioxide was measured. The indoor carbon dioxide was approximately 1100 ppm, e.g., in a cinema. The atmospheric carbon dioxide reached to a considerable level, e.g. 3800 ppm at the subway station that was crowded with many passengers. These results show that the atmosperic carbon dioxide has been increasing during these three years, because the atmospheric carbon dioxide in December, 1993 measured by us was as much as about 450 ppm in several main streets in Tokyo. These values are much higher than the mean values of the world (350 ppm; Berry and Colls 1990). It is conceivable that such increases in atmospheric carbon dioxide may be occurring throughout the world in large cities with air pollution, which may cause finally the increase in atmospheric carbon dioxide of the world.

Since atmospheric carbon dioxide has increased greatly in the past two years in Tokyo (Table 1), it is possible that such increment of atmospheric carbon dioxide causes the increase of bicarbonate concentration in bloods of the residents in Tokyo, resulting in the excessive excretion of urinary bicarbonate. This view was supported by the results in Fig. 1A and B. About a half century ago, it was reported that mean values of urinary bicarbonate and the pH of urine of normal adults were neglibible and around 5.5, respectively (Pitts et al. 1949; Becker et al. 1981). These values would have been be influenced by the low level of atmospheric carbon dioxide (300 ppm in 1950; Berry and Colls 1990). However, as shown in Fig. 1A and B, we found that urinary bicarbonate and pH were significantly increased in the students in Tokyo, 1995 and 1996. Such extensive increase of urinary bicarbonate has been shown to be observed in the metabolic alkalosis induced by the intravenous infusion of sodium bicarbonate (Portwood et al. 1959).

We consider that the increased level of urinary bicarbonate and pH of the students in Tokyo may be closely correlated with the increase of atmospheric carbon dioxide. This view is consistent with the report of Schwarz et al. (1959) that the excretion of urinary bicarbonate was increased in a dog that inhaled high levels of carbon dioxide gas. Our present results in Fig. 2 also indicate the involvement of the increased atmospheric carbon dioxide in the excess excretion

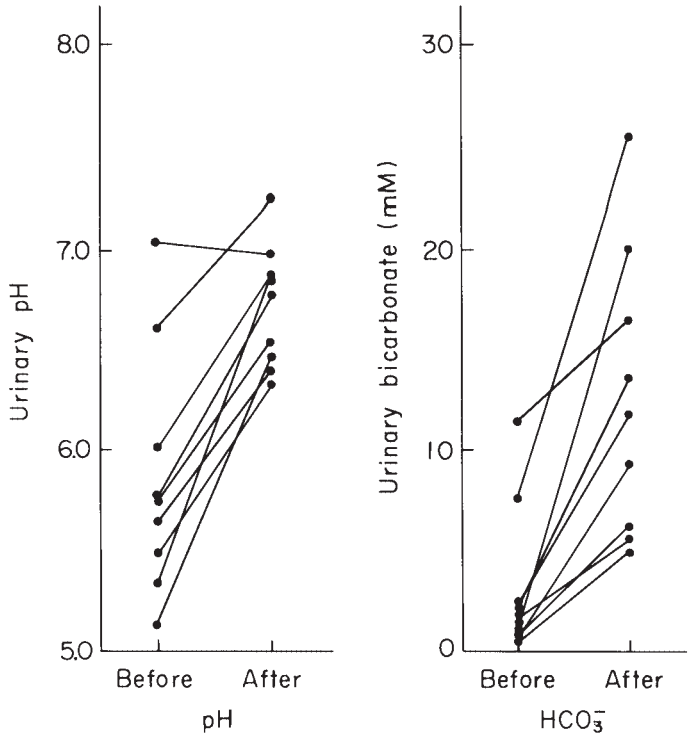

Fig. 2. Changes in urinary pH and bicarbonate concentration during the car trip by four or five students, with all windows closed, for 3 hours. Urine was collected before the start and after the end of the trip, and urinary bicarbonate and pH were immediately analyzed. Left column in the figure shows the changes in urinary pH before and after the trip. Right column in the figure shows the changes in urinary bicarbonate concentrations before and after the trip.

of urinary bicarbonate, because the increase in carbon dioxide in a car during 3-hour trip caused the extensive increase in urinary pH and bicarbonate. This result is consistent with our previous report on the increased urinary bicarbonate and pH of the students who stayed in a cinema for 3 hours (Tomoda et al. 1995).

The mechanism for the increase of urinary bicarbonate may be explained by the increased bicarbonate in blood caused through the action of erythrocyte carbonic anhydrase (Armstrong et al. 1966), resulting in the increased excretion of bicarbonate into urine (Pitts et al. 1949). According to Pitts et al. (1949), the excess bicarbonate was excreted into the urine, causing a concomitant rise in urine pH, when the level of bicarbonate in blood exceeded 28 mM, while the concentration of bicarbonate in blood was strictly maintained between 23 mM and 28 mM.

As stated above, it is likely that atmospheric carbon dioxide has increased greatly in these three years, in Tokyo. Since the same situation is probably present in many large cities throughout the world, techniques for preventing the release of carbon dioxide into the air are necessary, as soon as possible.

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