Humans have lived with countless microbes beginning with our primitive ancestors. However, microbes appeared much earlier in evolution than before our human relatives walked on the earth. In essence, it is the fate of humans that they are the tenants in the rented houses of the microbiological world. Interactions between humans and microbes have appeared in a variety of ways from killing humans by fatal rabies to aiding humans by gastrointestinal use of *Lactobacillus*. I love drinking beer and wine, especially at parties with good friends. Such alcoholic beverages are made with yeast, one of the oldest microbes to be found on the Earth. Our human ancestors have enjoyed alcohol for thousands of years. Not only beverages, but many foods are also made with microbes, including *natto* (fermented Japanese beans), cheese, and so on. Microbes are vital in our daily lives.

Microbes also help to maintain the human body. Normal flora in the intestines protect not only that environment but also the whole body. For example, vitamin K is produced from normal gut flora and helps the body to produce coagulation factors in the liver, which then curtails bleeding. Normal gut flora also eliminate pathological microbes such as *Clostridium difficile* infection, which can cause fatal pseudomembranous colitis. This dreadful infection occurs by colonizing the intestine, usually after a course of antibiotics, thereby preventing normal gut flora regrowth. A small randomized controlled trial of 39 patients with recurrent *Clostridium difficile* infection showed the striking finding that “feces” with healthy gut flora was the best treatment of resistant disease.\(^1\) The authors reported that initial oral vancomycin, followed by bowel lavage and subsequent infusion of a solution of donor feces through a nasoduodenal tube was superior to vancomycin treatment alone or vancomycin treatment with bowel lavage. This achieved resolution of the diarrhea associated with *Clostridium difficile* infection without relapse after 10 weeks (resolution rate 81%, 31%, 23%, respectively). From when humans first discovered Penicillin in 1929, we have developed a number of antimicrobial agents. However, the development of newer and stronger antimicrobial agents has always resulted in the breakage of both favorable and unfavorable interactions between humans and microbes. This report made us reevaluate that humans owe their lives to the favorable interactions between humans and microbes. In this issue of the *Journal*, two articles shed light on the relationship between humans and microbes and how to manage these interactions.\(^2,3\) Dental caries is...
one of the most common health problems in primary care with *Streptococcus mutans* being a frequent offender. Thus, control of this organism in the oral cavity is a way to keep our teeth healthier. Takayama et al. conducted a survey in 264 pregnant women focusing on their oral hygiene. They found that four out of five pregnant women had low proportions (<1%) of *Streptococcus mutans*, which were appropriate to reduce the risk of developing dental caries. As expected, oral health behavior, including tooth brushing time, consciousness brushing, and frequency of formal dental health care visits, was associated with a lower proportion of *Streptococcus mutans* colonization. It is inevitable to have selection bias in this type of study meaning that the enrolled pregnant women have more affluent lifestyles allowing them to participate in the investigation and as such, they are probably healthier than the general population. However, it supported the idea that healthy behavior is much more important than other measures, such as antiseptic mouth wash usage, even though there was no information regarding antiseptic mouth wash use during the study period.

Iwata and 23 colleagues reported the effect of a Chinese herbal medicine, Gingyo Gedokusan on 15 patients with influenza symptoms in a non-randomized clinical trial. The investigators administered Gingyo Gedokusan to 8 patients and oseltamivir in the other 7 patients according to the patients’ preferences. It was noteworthy that the mean time to resolution of symptoms was longer in Gingyo Gedokusan group than the oseltamivir group (3.9 days vs. 3.3 days) but the mean time to recovery of activity levels was in favor of Gingyo Gedokusan (3.3 days for Gingyo Gedokusan vs. 4.3 days for oseltamivir). Thus, the patients administered Gingyo Gedokusan returned to their usual activities before the symptoms resolved but their oseltamivir counterparts returned to their activities only after symptom resolution. These findings should be interpreted in respect of the non-randomized and open-label study design. In other words, it would appear that patients who received Gingyo Gedokusan may be more tolerant to influenza symptoms and who therefore feel better earlier to be able to return to their activities. It is meaningless to argue the differences in effects of Gingyo Gedokusan and oseltamivir, if any, from this study, but it was fact that 8 healthy adults recovered from influenza or influenza-like illness without receiving neuraminidase inhibitors.

Penicillin and other antibiotics have changed the treatment modalities against some kinds of diseases associated with microbes and have saved countless lives of healthy adults worldwide since their inception. Conversely, we do not have evidence that neuraminidase inhibitors have saved the lives of healthy adults since their development. Consider 18 years ago since I became a doctor. We did not have neuraminidase inhibitors but almost all patients including myself with influenza symptoms recovered within several days. With appropriate antipyretic therapy and rest (frequently we could not rest), these were the only treatment options available other than the off-label use of amantadine. For healthy adults, the only merit of the launch of neuraminidase inhibitors might be that physicians not longer had to yield under pressure to prescribe antibiotics for influenza symptoms. In that respect, it has undoubtedly reduced unnecessary antibiotics prescriptions. However, physicians now face the new pressure of prescribing the neuraminidase inhibitors.

We as primary care physicians, should be better at managing common health problems and be the gatekeepers of antimicrobial agents. We do not use antibiotics to control or prevent dental caries in daily practice. Patients or the general population accept that improved tooth brushing can prevent or delay dental caries, and they do not take antibiotics to suppress *Streptococcus mutans*. In the same way, we should educate patients and change the thinking of the general population. We see many health care problems, which are totally or partially associated with microbes. Upper respiratory infections (URI) including influenza-like illness, post-URI cough, acute diarrhea or enterocolitis are treatable without antimicrobial agents. Chinese herbal medicine might be one of the options to alleviate the concerns of patients when antimicrobial agents are not prescribed. Contamination or colonization of resistant strains of microbes in the normal flora are not the target of
antibiotics. This simple rationale is often ignored and many managers of nursing homes request physicians to eliminate such strains found from the elderly residents by chance. It is one of the roles of primary care physicians to manage health problems rationally, even if they are associated with microbes.

References