per oil increased cerebral blood flow in the right anterior cingulate cortex and the left insular cortex (29), which is impaired in patients with aspiration pneumonia (26).

Since olfactory stimulation using essential oil is inconvenient for the caregiver and conducting daily aromatherapy is a large caregiver burden, we developed an easier method to conduct black pepper aromatherapy using a new drug gas delivery system (DGDS) (31). DGDS is a novel drug delivery system of transdermal absorption, which takes a volatile bioactive component into the body in a gaseous condition safely and steadily. It was developed as a technology that can safely administer a volatile component (terpenoid) of a plant secondary metabolite. The aroma component of black pepper is continuously transported to the target for 24 h by a DGDS used for black pepper essential oil (Fig. 3). This sheet easily and stably provides olfactory stimulation using the aroma component of black pepper oil by changing the aroma patch sheet daily (31). It is almost equally as effective as direct black pepper oil stimulation. We experienced many cases of refractory pneumonia in the elderly treated with many antibiotics, whose swallowing reflexes were restored by the application of black pepper oil DGDS (black pepper aroma patch sheet) (Fig. 4).

6. Oral care and cough and swallowing reflex

Oral care has been recognized as helping to keep the bacteria in the mouth, thereby preventing aspiration pneumonia. Yoneyama et al. (32, 33) showed significant results in reducing aspiration-induced pneumonia when professional dental hygienists came to nursing facilities on a regular basis. We investigated the effects of oral care on airway protective reflexes and found that one-month daily oral care significantly improved both swallowing and cough reflexes in the elderly nursing home patients (34). Our data suggest that oral care may reduce the risk of pneumonia by improving the swallowing reflexes and by improving overall functional status. Tooth brushing, pain stimuli to gingiva, is known to activate the insular cortex in a functional MRI study (35). Since the insular cortex function is impaired in patients with aspi-

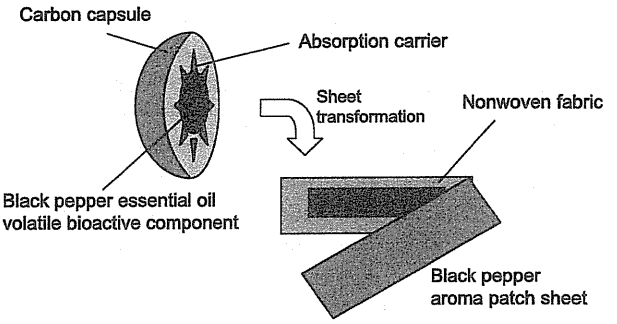

Fig. 3. Development of new drug gas delivery system (DGDS) (Aroma Patch) to provide olfactory stimulation using black pepper with less burden to the caregiver.

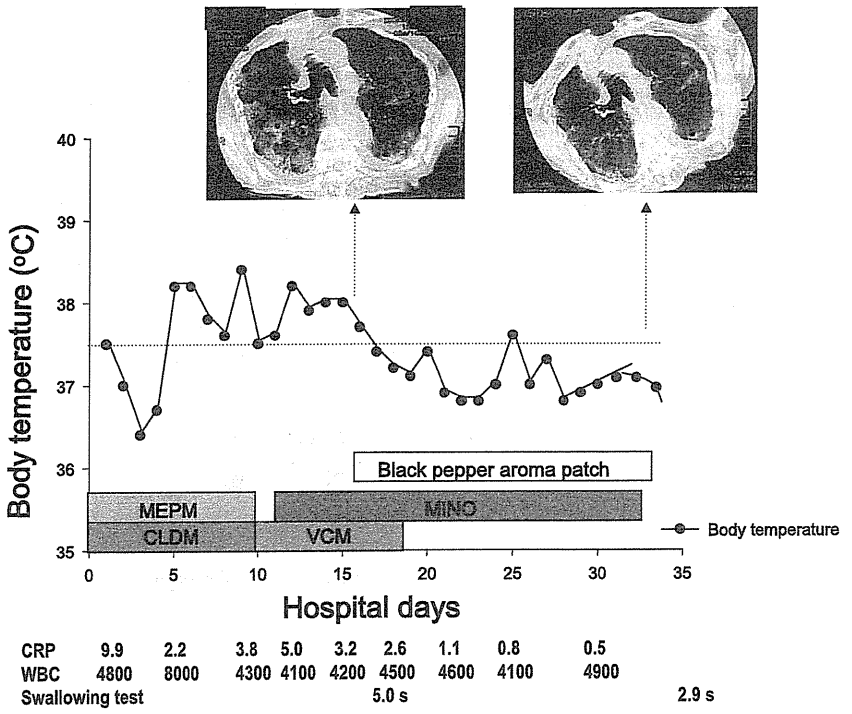

Fig. 4. A case of a black pepper aroma patch sheet use for the elderly with intractable pneumonia due to aspiration. MEM: Meropenem, CLDM: Clindamycin, VCM: Vancomycin, MINO: Minomycin.

ration pneumonia and severe dysphagia (26), we speculate that repeated oral nociceptive sensory stimulation may restore the function of insular cortex, resulting in restoration of the functions of the swallowing reflex.

7. Future perspectives

In addition to TRPV1 and TRPM8 agonists, there might be other food components with the ability to improve swallowing function. For example, we found that red wine polyphenol improve the swallowing reflex by modulating the TRPV1 response (36). The study by Watando et al. (21) suggests that TRPA1 agonists such as allyl-isothiocyanate (wasabi) and cinnamaldehyde (cinnamon) may be beneficial for the swallowing reflex; Further research is needed to uncover the effects of these agonists. Oral care and swallowing rehabilitation are also known to improve the swallowing function and prevent aspiration pneumonia in the elderly (34). Since the aspiration pneumonia in the elderly is often very refractory (37), we should put all these remedies together in the treatment and prevention of aspiration pneumonia. Patients with severe aspiration pneumonia are usually given nothing to eat at the time of admission to the hospital. The most important and challenging step in aspiration pneumonia treatment is restarting eating after recovery using antibiotic treatment. We developed a protocol to restart eating in patients with feeding and swallowing disorders by a combination of aromatherapy, spices, oral care, and swallowing rehabilitation (31). Implementation of this protocol helped avoid re-aspiration as well as gastrostomy in many elderly people.

The shift in demographic composition is supposed to raise the costs of nursing home care service. Prescription drug spending for the elderly is increasing. Research on how to manage the frail elderly is crucial not only for medical but also for economic reasons.

Acknowledgments

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Cough in the elderly: A novel strategy for preventing aspiration pneumonia

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ABSTRACT

Management of cough in the elderly with a deteriorated physical and mental status has received little focus. Since an aged population is rapidly increasing in developed countries, the research in this population are warranted. Cough reflex sensitivity in the elderly was shown to be hypersensitive, normosensitive and hyposensitive. The hypersensitive cough reflex is mostly due to gastro-esophageal reflux in nursing home patients. Impaired cough reflex sensitivity is assumed to play a crucial role in the development of pneumonia in the elderly. A marked depression of cough reflex sensitivity is reported in elderly patients with aspiration pneumonia. The impairment of the cough reflex in patients with aspiration pneumonia can involve both cortical facilitatory pathways for cough and medullary reflex pathways. We found the urge-to-cough in patients with aspiration pneumonia was also down-regulated, suggesting the involvement of supramedullary dysfunction in the etiology of aspiration pneumonia in the elderly. In order to prevent aspiration pneumonia in the elderly, restoration of cough reflex sensitivity is essential. We found several methods to restore cough reflex sensitivity in the elderly. They also improved the swallowing reflex, another important airway protective reflex, in the elderly. In the treatment of aspiration pneumonia, one of the most challenging steps is the start of eating for patients who usually fast at the time of hospitalization. By combining the methods to restore the cough reflex sensitivity and swallowing reflex, we developed a protocol to start eating in the elderly patients with aspiration pneumonia. Using the protocol, we reduced the incidence of re-aspiration due to start of eating in patients with aspiration pneumonia to one third of the patients without the protocol.

1. Introduction

The aged population in developed countries is increasing very rapidly and the proportion of the population that is elderly is dramatically rising over the decades. Therefore, research concerning how to manage an aged population is an urgent research subject [1]. However, the management of cough in the elderly with a deteriorated physical and mental status has received little focus.

When the distribution of cough reflex sensitivities were estimated by citric acid inhalation in 123 elderly nursing homes residents (mean age: 84.4 [SD: 5.6] yrs), we found a wide range distribution, which we can classified into three groups: hypersensitive ($n = 20$), normosensitive ($n = 73$), and hyposensitive ($n = 30$) group [2]. The investigation of esophageal endoscopy, 24-h pH monitoring and effect of a proton-pump inhibitor (PPI) in the cough reflex hypersensitive group in cough reflex hypersensitivity group suggests the contribution of gastro-esophageal reflux to the hypersensitivity. PPI medication might be a primary remedy for persistent cough in the elderly with a depressed physical and cognitive status.

Elderly people with cough reflex hyposensitivity are supposed to be more crucial people to be identified in terms of prognosis because the impairment of cough reflex is related to life-threatening pneumonia. Pneumonia in the very old is often refractory. In spite of strong antibiotics, sometimes it progresses, suggesting we need another strategy to treat this. Despite the development of strong antibiotics, pneumonia hospitalization is increasing in many developed countries [3]. Among the people who die of pneumonia, most of them are elderly people. The result of a multicenter survey which investigated the ratio of aspiration pneumonia among hospitalized pneumonia showed that the ratio of aspiration pneumonia is very high in older people [4]. Therefore, in this article, we mainly focused on protective reflexes and aspiration pneumonia in the elderly.

2. Protective reflexes and aspiration pneumonia in the elderly

Adequate protective reflexes in the airway are important to prevent aspiration pneumonia, and the suppression or absence of these reflexes is a major risk factor for its development. For example,

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Nakajoh et al. [5] reported that the incidence of pneumonia was higher in patients having both a latency of swallowing response longer than 5 s following stimulation and a cough threshold for inhalation of citric acid aerosol higher than a concentration of 1.35 (log mg/mL). Thus, the impairment of protective reflexes (i.e. swallowing and cough reflexes) is thought to be one of the major mechanisms for aspiration pneumonia in older people, which is often seen in older people [6]. In fact, impaired swallowing and cough reflexes have been shown in patients suffering from aspiration pneumonia [7].

Although the progressive loss of the protective reflexes with age has been postulated in aged people, elderly people who lead active daily lives have shown that both reflexes do not decrease with the advanced of age [8,9], suggesting that factors affecting activity of daily living (ADL) contribute to the impairment of protective reflexes. Disorders of the central nervous system, which often deteriorate ADL, are very likely to develop in the elderly.

Up to a half of the stroke patients studied with videofluoroscopic evaluation of swallowing have dysfunctional swallowing [10], and a third of these dysphagic patients aspirate [11,12]. Pneumonia develops in more than one third of aspirators, and 3.8% of patients die as a result of this complication [13]. Sekizawa et al. [14] published a landmark study showing a lack of cough reflex in elderly patients with aspiration pneumonia. Since the authors did not distinguish cough reflex and expiration reflex in this study, lack of cough reflex indicated the absent of both cough and expiration reflexes. Using stimuli specific to expiration reflex, Addington et al. [15] showed the expiration reflex was absent or weakened in post-stroke patients, leading to aspiration pneumonia. Voluntary cough has also been shown to be weakened in post-stroke patients, which is also shown to be related to aspiration pneumonia [16,17].

In addition to ischemic CNS disease, degenerative CNS diseases which elderly people often suffer from were also shown to deteriorate protective reflexes. The main cause of death in patients with Parkinson's disease is aspiration pneumonia [18], which leads to the suggestion that cough and swallowing function is impaired in this condition allowing aspiration. Dysphagia is a frequent and potentially serious complication of Parkinson's disease [19]. Potulska et al. [20] demonstrated delayed triggering of the swallowing reflex, prolongation of laryngeal movement, prolongation of the esophageal phase of swallowing in patients with Parkinson's disease. Fontana et al. [21] showed that the intensity of cough was depressed, indicating the motor defect of cough in Parkinson's disease. Later, we showed that, while the change in early Parkinson's disease corresponds to motor defects, in more advanced Parkinsonism a sensory defect developed [22].

3. Order of impairment between swallowing and cough reflexes

Although both reflexes are important airway protective reflexes, it seems to have an order of impairment. By estimating the two protective reflexes, Nakajoh et al. [5] graphed the distribution of both swallowing and cough reflex sensitivities in a post-stroke nursing home residents and showed that there are residents whose swallowing reflex is impaired whereas cough reflex is maintained whereas there are few residents whose swallowing reflex is intact and cough reflex is impaired. The results suggest an impaired cough reflex subsequent to swallowing reflex in post-stroke patients. This order also seems to be preserved in Parkinsonism. Volonté et al. [23] reported that the impairment of swallowing reflex was observed but the impairment of cough reflex was not in the early stage of Parkinson's disease. Since patients with early Parkinson's disease are less likely to have aspiration pneumonia, the simultaneous impairment of protective reflexes occurs at an advanced stage. Smith and Wiles [24] reported that patients with neurogenic dysphagia, including patients with Parkinson's disease, did not have a reduced cough reflex sensitivity. Taken together, it can be speculated that impairment of swallowing reflex was succeeded by impairment of cough reflex in the majority of the elderly. A recent large scale study by Mitchell et al. [25] supports the idea. In patients with advanced dementia in nursing homes, there is more than a 1-year time lag between the start of an eating problem and suffering from pneumonia. Thus, the combination of impaired swallowing and cough reflex plays a crucial role in developing aspiration pneumonia.

4. Supramedullary mechanism of cough reflex impairment in aspiration pneumonia

Addington et al. [26] determined the effect of identifying initial anatomical radiological stroke location on the laryngeal cough reflex test result. They found a significant relationship among the laryngeal cough reflex test result, pneumonia risk and both brainstem and cerebral hemispheric infarctions. Since anatomical radiological stroke location is not necessarily the functional neuroanatomical site responsible for the abnormality, the functional neuroanatomical site preferentially involved in aspiration pneumonia should be elucidated. By using a single photon emission study, we found significant cerebral blood flow reduction in the bilateral anterior insular compared with the group without a history of pneumonia, suggesting the involvement of dysfunction of the bilateral insular cortex in impaired cough reflex sensitivity [27].

The impairment of cough reflex in patients with aspiration pneumonia could be attributed to both cortical facilitatory pathways for cough and medullary reflex pathways [28]. A recent functional magnetic resonance imaging study revealed that the urge-to-cough was associated with activations in a variety of brain regions, including the insular cortex, anterior midcingulate cortex, primary sensory cortex, orbitofrontal cortex, supplementary motor area, and cerebellum [29]. Since the dysfunction of the insular cortex in aspiration pneumonia was a supramedullary event, we evaluated the urge-to-cough in patients with aspiration pneumonia in order to study the possible involvement of the supramedullary system in the down-regulation of the cough reflex [30]. We found that the urge-to-cough is significantly attenuated in elderly patients with aspiration pneumonia, suggesting the involvement of supramedullary dysfunction in the etiology of aspiration pneumonia in the elderly.

Since cough starts with a deep inspiration which would cause aspiration, the main reflex that prevents aspiration might be the expiration reflex from the glottis. The loss of expiration reflex from the larynx, possibly leading to aspiration and to pneumonia, is thought to be a medullary misfunction, since the reflex has too short a latency from the sensory receptor to expiratory muscle (mean 17.6 ms) to allow direct involvement of the cortical pathway [31]. However, there is a possibility that the cortical pathway modulates sensitivity of expiration reflex. Aspiration of small amounts of oropharyngeal secretions without an overt sign, so-called silent aspiration, is a common and non-transcendent physiological phenomenon which mainly occurs during sleep. Even normal healthy aged people reportedly do not swallow for periods of more than 30 min during the night, and secretions that accumulated in the laryngopharynx during this time are aspirated [32]. Continuous aspiration to the pharynx at night may induce tonic activation of urge-to-cough sensation, subsequently resulting in lowering both the cough and expiration reflex threshold by cortical modulation (Fig. 1). The cortical dysfunction involving urge-to-cough might disrupt occasional airway cleaning, leading to aspiration pneumonia.

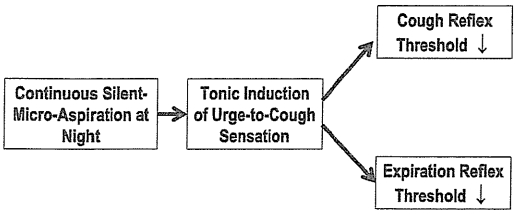

Fig. 1. Possible mechanism that urge-to-cough affect expiration and cough reflex sensitivities.

5. Importance of temperature of food to prevent aspiration

Although silent aspiration at night is an important cause of aspiration pneumonia, the aspiration related to food intake still remains a crucial issue. Therefore, dietary modification is a common management approach to prevent aspiration. Since patients vary in their ability to swallow thin and thick liquids, semi-solid and solids, the consistency of the patients food is recommended according to the assessment of the ability to swallow. Various consistencies for diet to choose include: level 1 (puree), level 2 (soft liquids), Level 3 (chopped items), level 4 (all foods, except sliced beef, poultry, bread), and level 5 (regular) [33]. Heretofore, dietary modification to help swallow has focused only on texture matters such as inconsistency and thickness. However, a meal has a plenty of elements other than texture (Fig. 2). All of these elements should be modified to help dysphagic people easily swallow. Among the elements of meal, we first focused on the temperature.

We found that the swallowing function of elderly people is temperature sensitive even though the function is impaired. Fig. 3 shows the schematic relationship between the various temperatures of infused distilled water. The swallowing reflex was delayed the most around body temperature (30–40 °C) and the delay shortened as the difference in temperature apart from body temperature [34]. The results of this research suggest it is important to provide a variety of temperatures when serving meals. Food should be prepared immediately prior to consumption. Pre-made meals should not be provided without being properly heated. Food needs to be heated in a microwave oven just before eating. Since elderly people take time to eat, nabe-mono, a one-pot dish cooked at the table, or meat grilled on a hot plate are ways to stimulate the appetite and improve nutrition while providing an appropriate food temperature.

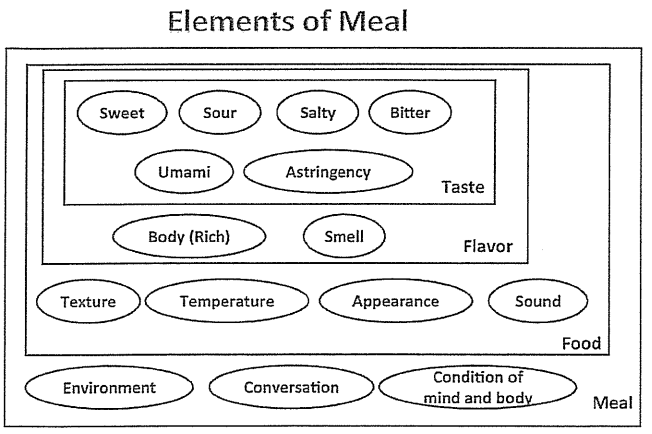

Fig. 2. Elements of meals.

6. TRP thermoreceptors and cough and swallowing reflexes

The reception of outer temperature is carried out by peripheral sensory nerves that convert the temperature stimuli into electric signals which are then transmitted to the central nervous system. Mammals have 6 TRP channels on the peripheral sensory nerves which are related to the reception of temperature; TRPV1, TRPV2, TRPV3, TRPV4, TRPM8 and TRPA1. Each has a different activation temperature threshold (TRPV1 > 43 °C, TRPV2 > 52 °C, TRPV3 > 32–39 °C, TRPV4 > 27–35 °C, TRPM8 > 25–28 °C and TRPA1 > 17 °C) [35]. As shown in Fig. 4 (below), TRPV1, TRPV2, TRPM8, and TRPA1 may be related to activation of the swallowing reflex.

It has been shown that the swallowing reflex temporally improves due to acute stimulation of TRPV1 [36]. Therefore, whether the swallowing reflex would continuously improve due to chronic stimulation of TRPV1 was examined using a troche containing capsaicin, which is a TRPV1 agonist and most common tussive agent for cough challenge test. When nursing residents were randomly divided into two groups and a capsaicin pastille or placebo was administered to each group for one month, the intervention group showed significant improvement in swallowing and cough reflexes [37]. This shows that chronic stimulation of TRPV1 in the mouth and pharyngeal region improved swallowing and cough reflexes. Therefore, the administration of a capsaicin pastille may prevent aspiration pneumonia in elderly people.

We also showed swallowing improvement by stimulation of cold receptor TRPM8. Menthol, the main element of mint, was considered to provide a cool sensation. TRPM8, a cool/cold stimulation receptor gene was cloned as TRPM8, menthol receptor. Therefore, we infused a menthol solution of 10^{-4} M, 10^{-3} M, or 10^{-2} M, or ice cold water into elderly people with delayed swallowing reflex to measure the swallowing reflex. Delayed swallowing reflex shortened depending on the dose of menthol [38]. This suggests that drug therapy using menthol may show the same effects as physiotherapy known as thermal stimulation [39], which is currently used in rehabilitation of swallowing disorders. Furthermore, food which includes menthol may be applicable for swallowing training. Menthol is much used as a cough depressant in general. There are patients whose swallowing reflex is impaired but their cough reflex is hypersensitive rather than impaired. Menthol might be a remedy for such patients.

The mechanism of why chronic stimulation of thermoreceptors improve swallowing and cough reflexes is speculative. Afferent neuronal pathways provide for discriminative sensation and for homeostatic control of body temperature. In discriminative sensation, the lamina-I neurons carry temperature signals to the final insular cortex with one or two relays [40]. Since we found that the function of the insular cortex is impaired in patients with aspiration pneumonia, we speculate that repeated thermoreceptor stimulation may restore the function of the insular cortex, resulting in restoration of the functions of swallowing reflex and cough reflex.

7. Oral care and cough and swallowing reflex

Oral care has long been recognized as helping to keep the bacteria in the mouth, leading to preventing pneumonia. Yoneyama et al. [41,42] reported significant results in reducing aspiration-induced pneumonia when professional dental hygienists came to nursing facilities on a regular basis. There are also some good studies in critical care nursing areas [43] who have shown that the incidence of ventilator-dependent pneumonia is drastically decreased with aggressive oral care in intensive care patients. In a study by Yoneyama et al. [42], they showed the incidence of pneumonia was equally inhibited to half both in edentate and dentate. Since the

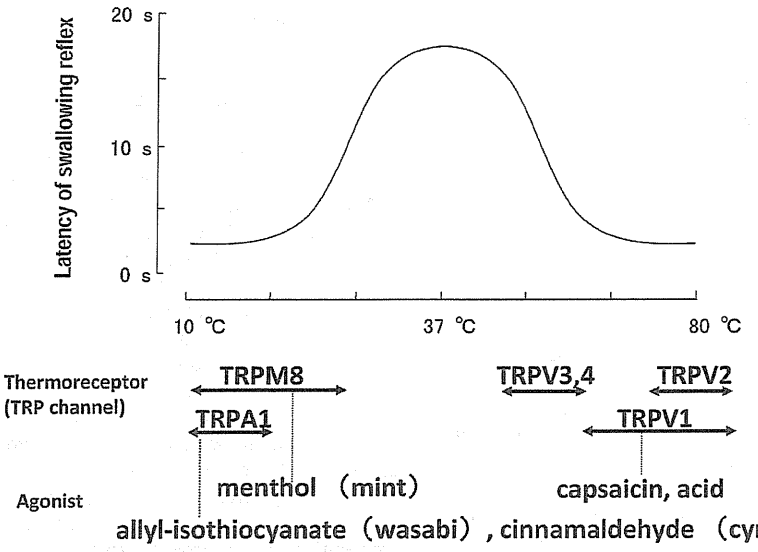

Fig. 3. The relationship between temperature of swallowed material and latency of swallowing reflex. The lower panels show the temperature covered by each TRP thermoreceptor, and its agonist food.

bacteria are mainly located around teeth, the cleaning bacteria may not be the only mechanism to prevent pneumonia by oral care. Therefore, we investigated the effects of oral care on airway protective reflexes and found that one month daily oral care significantly improved both swallowing and cough reflexes in the elderly nursing home patients [44,45]. Our data suggest that oral care may improve the swallowing reflex and the ability to perform ADLs among elderly patients. The elevated substance P levels in the oral care group suggest that daily brushing stimulates sensory nerves in the oral cavity by enhancing release of neuropeptides, through afferent or efferent pathways of the swallowing reflex. Oral care may reduce the risk of pneumonia by improving the swallowing and cough reflexes and by improving overall functional status. The elevated substance P levels in the oral care group suggest that daily brushing stimulates sensory nerves in the oral cavity by enhancing release of neuropeptides, through afferent or efferent pathways of the cough and swallowing reflexes. Toothbrushing, pain stimuli to gingiva, is known to activate the insular cortex in a functional MRI study [46]. Again, the insular cortex function is impaired in patients with aspiration pneumonia and severe dysphagia [27]. We speculate that repeated oral nociceptive sensory stimulation may restore the function of insular cortex, resulting in restoration of the functions of swallowing reflex and cough reflex.

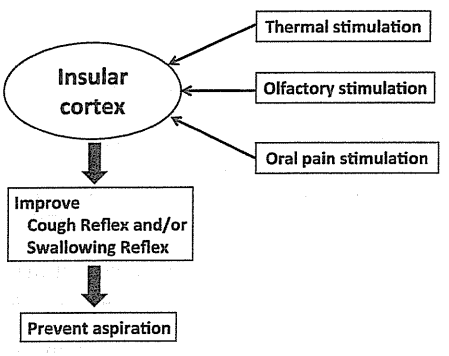

Fig. 4. Sensory stimuli and airway protective reflexes.

8. Swallowing improvement by olfactory stimulation using black pepper

Internal medicine or food to improve dysphagia patients is not applicable for individuals at risk of aspiration with low ADLs or decreased consciousness. Therefore, olfactory stimulation is proposed to improve feeding and aspiration of elderly people who cannot orally consume food [47]. Nursing residents were randomly divided into three groups (black pepper, lavender, and no smell). For one month, each group received 1-min of olfactory stimulation of black pepper, lavender or no smell before every meal. Swallowing reflex, cough reflex and the substance P concentration in peripheral blood before/after the intervention of olfactory stimulation were measured [48]. Swallowing reflex and substance P concentration significantly increased after olfactory stimulation using black pepper stimuli. There were no significant improvements in cough reflex. Olfactory stimulation using black pepper may be an effective method to treat feeding and swallowing disorders and to prevent aspiration pneumonia.

In a single photon emission tomography study, we found that olfactory stimulation with black pepper oil increased cerebral blood flow in the right anterior cingulate cortex and the left insular cortex [48]. We found a bilateral impairment of the insular cortex in repeated-aspiration pneumonia [27]. The result may suggest that, in order to restore the cough reflex, one side activation of insula cortex may not be enough. Further studies are needed.

9. Protocol to restart eating

Patients with severe aspiration pneumonia usually fast at the time of admission. In the treatment of severe aspiration pneumonia, the most important and challenging step is to start eating after recovery using antibiotic treatment. As described above, we found three sensory stimuli which activate the insular cortex and they have ability to restore the cough reflex or swallowing reflex in the elderly (Fig. 4). Using these sensory stimuli, we developed a protocol to start eating more efficiently and safely. The intensive stepwise method to start oral intake advocated is in Fig. 5. Oral feeding of older adults was postponed until their pneumonia was confirmed to

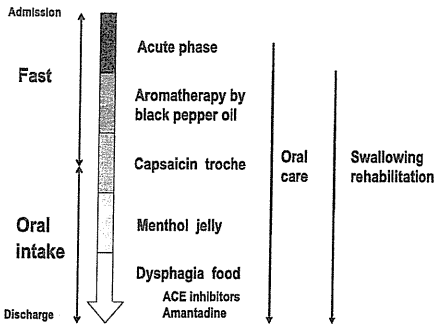

Fig. 5. Protocol for start of oral intake with prevention of re-aspiration in patients with aspiration pneumonia.

be cured. Soon after patients were judged to be nearly cured of pneumonia, aromatherapy with black pepper oil was started as the first step. The second step was the additional application of capsaicin troches, three times per day 3 days after the start of aromatherapy with black pepper oil. The third step was that jelly including a menthol ingredient (menthol gel) was provided as the first meal when eating was resumed 5 days after the addition of the capsaicin troches. If patients were able to swallow the menthol jelly safely, they were provided in a step-by-step manner with the proper food texture depending on their ability to swallow such food as paste or pudding or usual meals including liquids and solids. Using this protocol, the incidence of pneumonia and the number of febrile days for 1 month from the start of oral intake were significantly reduced [49]. Implementation of this protocol would help avoid gastrostomy in many elderly people. In addition, this protocol is also applicable to feeding training and rehabilitation of all feeding and swallowing disorders.

10. Conclusions

As physicians, it might be very important for us to make every effort to encourage oral intake, considering the safety as well as the efficiency to sustain patients. Assessment by a clinical dietitian and nutritional supplementation may be important. Tube feeding is not essential in all patients who aspirate. The risk of aspiration continues after placement of the gastrostomy tube [50,51]. An extensive review of articles in Medline between 1966 and March 1999 on the effects of tube feeding on the outcome of patients with dementia by Finucane et al. [52] did not find relevant data supporting the conjecture that tube feeding prevents aspiration pneumonia. They and other investigators also could not find data that demonstrated a survival benefit with tube feeding [53].

The mechanism of aspiration pneumonia is in part explained by the substance P theory [54,55]. As dopamine production in the corpus nigrostriate may be decreased in patients with cerebral infarction, particularly in those with multiple and bilateral infarction, decreased dopamine production may reduce the expression of substance P at the glossopharyngeal nerve and at the cervical parasympathetic ganglion of the sensory branch of that nerve [56,57]. The depression of substance P is thought to be associated with impairment of swallowing and cough reflexes, resulting in aspiration pneumonia [58]. However, these studies confused cough reflex and expiration reflex, which is a main reflex that should prevent aspiration. Therefore, we have to carefully re-think this mechanism in terms of expiration reflex.

In view of the importance of cough and other defensive reflexes in maintaining successful human aging, far more research concerning the impairment of cough is needed.

Acknowledgements

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12 高齢者の口腔ケアと誤嚥の包括的管理

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Key words 口腔ケア 誤嚥性肺炎 誤嚥 抗誤嚥薬

はじめに

2010年発表の日本人平均の寿命は，男性79歳，女性86歳であり，その死因は1位悪性新生物(30％)，2位心疾患(16％)，3位脳血管疾患(11％)，4位肺炎(10％)である．この統計を65歳以上に限ると，肺炎(14％)，脳血管障害(11％)と，3位と4位が入れ替わる．2009(平成21)年度版高齢者社会白書によると，介護保険要介護者の原因は脳血管疾患が23％で1位である．これは死因における肺炎の増加傾向は，高齢者や障害者の誤嚥性肺炎の増加によるものと推測できる．つまり，高齢者肺炎の主体は誤嚥性肺炎であろうと考えられる．

1999年に，静岡県で開業している米山歯科医師らによって，口腔ケアが肺炎を予防するというエビデンスのある研究が発表された[1]．米山歯科医師らは，1週間に1回の歯科衛生士による口腔ケアをしたグループとしないグループの2年間の肺炎の発生率，発熱の頻度と死亡率を調べた．その結果，口腔ケアをしたグループはそうでないグループに比べ，肺炎の発生率が半分となることがわかった．

以上のことより，口腔ケアが誤嚥性肺炎を予防することが示唆されたわけである．

口腔ケアの肺炎予防機序

誤嚥性肺炎予防の機序については長らく，口腔ケアによる口腔内細菌の清掃が主と考えられてきた．高齢者の食事，排泄，入浴等で多忙な在宅や看護・介護の現場においては，口の中の清掃はおざなりにされやすく，口腔内が不潔な方が多くなっている．したがって，それを清潔にすることが，細菌の誤嚥の予防になるという考え方である．しかしながら，常に口腔を半開きにしている高齢者には常に口腔内に空中の浮遊細菌が降り注いでいる．また，口腔内の清掃の主なターゲットは歯周の細菌であり，それは残存歯の周囲に存在する．近年のデータによると，口腔ケアは歯のある高齢者も歯のない高齢者も同様に肺炎を半分にすることが報告されている．このことから筆者らは口腔ケアの高齢者の肺炎抑制の機序は，口腔内細菌の

清掃以外に要因があるのではと考えた．

誤嚥性肺炎発症の機序

2009年の「New England Journal of Medicine」誌にMitchellらにより施設入所の認知症高齢者の自然経過に関する大規模研究が報告された[2]．これによると，認知症高齢者は時間経過とともに8割まで嚥下障害(eating problem)が出現していて，そのような高齢者は約1年後に発熱，肺炎，死亡を起こしている．以上のことは，嚥下障害が出現しただけで，すぐに誤嚥性肺炎になるのではなく，その次の要因が重なって誤嚥性肺炎発症となることを示唆しているものと思われる．

筆者らの教室で行った施設高齢者の嚥下反射と咳反射を調べた研究において[3]，その分布を同時にみてみると，施設入所高齢者で肺炎を起こしている人は嚥下反射と咳反射の両方が障害されていた(図1)．嚥下反射が障害されていて，咳反射が保たれている高齢者は肺炎を起こしてなかった．また，咳反射が障害されているが，嚥下反射が保たれている高齢者はいなかった．この事実は2つのことを示唆している．1つには，誤嚥性肺炎は嚥下反射と咳反射という2つの気道防御反射が両方とも障害されることにより発症するということ．もう1つは，通常の高齢者の自然経過としてこの2つの気道防御反射のうち，まず嚥下反射が不可逆性に障害されて，その後，咳反射が障害されるということである．

以上のことより，高齢者はまず嚥下反射が障害されて，次に咳反射が障害されて誤嚥性肺炎になるということがわかってきた．

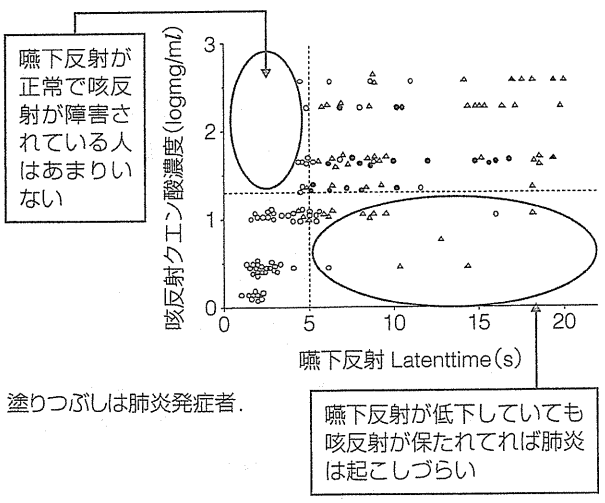

図1　施設入所高齢者の嚥下反射・咳反射と肺炎発症の関係の調査

口腔ケアの気道防御反射に対する効果

上記のことより筆者らは気道防御反射に対する口腔ケアの影響を調べた．まず，筆者らは口腔ケアが高齢者の遅延した嚥下反射に及ぼす影響を調べた[4]．すると，口腔ケアは嚥下反射を10日目ぐらいから改善することが判明した(図2)．それに伴い，口腔ケアにより高齢者のADLも改善することがわかった．さらに，口腔ケアが高齢者の咳反射に及ぼす影響を調べたところ[5]，咳反射も改善することがわかった(図3)．なぜ口腔ケアが

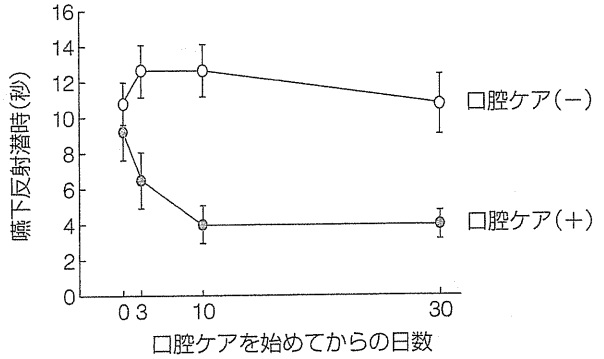

図2　口腔ケアの高齢者の嚥下反射に対する効果

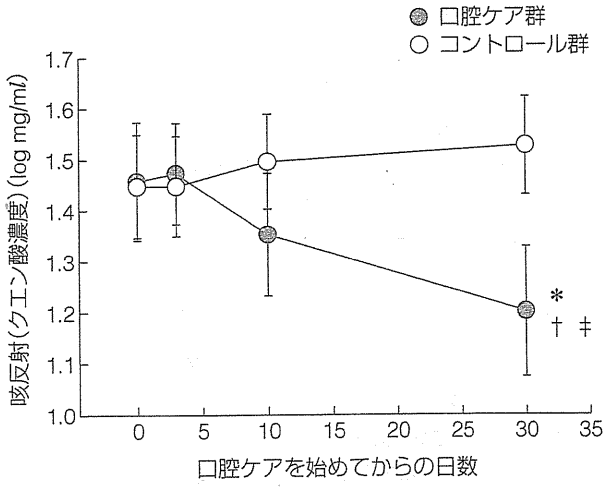

図3　口腔ケアの高齢者の咳反射に対する効果

高齢者の気道防御反射を改善するのだろうか？このメカニズムとして筆者らは，ブラッシングによる口腔の知覚(痛覚)刺激が，大脳の島皮質を活性化することによると考えている．というのは，誤嚥性肺炎を繰り返す患者においては嚥下と咳両方にかかわりが深い島皮質の活性が低下していることがわかっており，痛覚刺激求心路の投射のひとつが大脳島皮質であるからである．

このことより，口腔ケアが誤嚥性肺炎を予防する機序は，口腔ケアが高齢者の嚥下反射と咳反射の両方を改善するからと考えられる．

口腔ケア以外の誤嚥対処法

要介護高齢者における誤嚥の予防には口腔ケアだけでは不十分である．よく知られたトロミ等の食事の工夫とともに，抗誤嚥薬の投与を考え包括的に行うことが重要である．老年医学研究の進歩からさまざまな抗誤嚥薬とよべるものが登場している．嚥下の神経制御は末梢の知覚神経から大脳皮質まで末梢中枢神経全体で制御されている．それらに嚥下の神経性制御の階層性と，それぞれの抗誤嚥薬の作用部位を図4に示す．現在のところ，温度感受性TRP受容体作動薬，黒胡椒精油，シロスタゾール，アマンタジン，テオフィリン，ACE阻害薬等が日常臨床にて使用されている．TRP受容体作動薬は末梢神経と中枢神経の両方に作用し，それにはカプサイシン，メンソール，カプシエイト，赤ワインポリフェノール等がある．

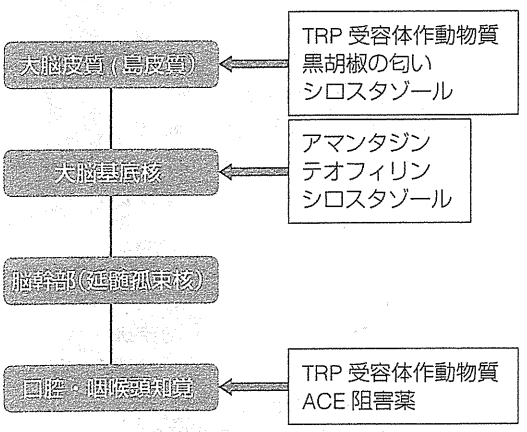

図4　嚥下の神経制御階層と抗誤嚥薬

誤嚥性肺炎患者の経口摂取開始包括的プロトコール

重症の誤嚥性肺炎の患者が入院したときは基本的に絶食である．抗生剤等の治療により患者さんが回復したとき，食事を開始する過程が実は誤嚥性肺炎の治療において最も重要でかつチャレンジングなステップである．そこで，安易に食事を開始したときに再誤嚥となり，それを繰り返すことにより耐性菌が発生したり，衰弱したりして経口摂取を諦めるようになり，胃瘻となったりする．胃瘻をつくったからといって誤嚥性肺炎が防げるわけではない．そこで，これまでの高齢者の嚥下機能回復法を包括的に集結した誤嚥性肺炎患者の食事開始プロトコールを立案した(図5)．このプロトコールを重症の誤嚥性肺炎の患者が入院し，点滴治療により回復し，食事を開始するときに採用することにより，筆者らの病棟では食事再開後の再誤嚥性肺炎の発症が3分の1に減少したのである[6]．

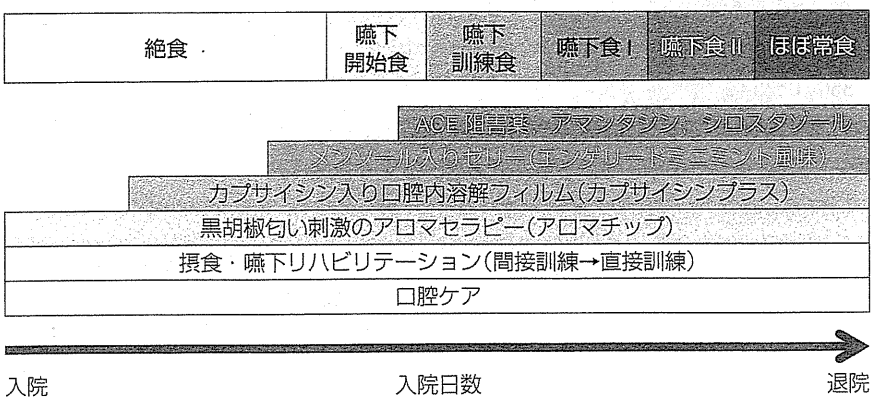

図5　誤嚥性肺炎患者の経口摂取開始包括的プロトコール

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開催案内

◎社団法人日本離床研究会主催 教育講座 脳内の革命！ 自分の脳も変えられる脳卒中セミナー

【日　時】2012年1月7日(土)14：30～18：00
1月8日(日)9：50～16：00
【会　場】お茶の水女子大学(東京都文京区)
【事務局】社団法人日本離床研究会
TEL：03-3350-0526
URL：http://www.rishou.org/

◎社団法人日本離床研究会主催 教育講座 シリーズ循環 臨床編 ライブ感覚で学ぶ！ 離床のできる循環相談所

【日　時】2012年1月7日(土)13：00～16：30
1月8日(日)9：40～16：00
【会　場】エル・おおさか(大阪市)
【事務局】社団法人日本離床研究会
TEL：03-3350-0526
URL：http://www.rishou.org/

◎第35回日本リハビリテーション工学協会 車いすSIG講習会 in 高知

【日　時】2012年1月28日(土)～29日(日)
【会　場】高知県立ふくし交流プラザ
〒780-8065 高知市朝倉戊375-1
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URL：http://www.fukushi-plaza.jp/index.html
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TEL：045-473-0666
FAX：045-473-0836
URL：http://www.wheelchair-sig.jp

◎アメリカ足病医学会のバイオメカニクスに基づく 足部の評価と運動制御アプローチ(3日間コース)

【日　時】2012年2月18日(土)9：00~18：30
19日(日)9：00～18：00
3月11日(日)9：00～17：30
【会　場】大浜第一病院会議室(那覇市)
【事務局】長野リハビリテーション研究会「ACT」
長野県中野市田上1164
URL：http://naganoact.ehoh.net

≪高齢者特有の症状に対応する——老年症候群≫
嚥下困難と抗誤嚥薬

海老原 覚　　海老原孝枝*

要旨

- 嚥下困難は，誤嚥や栄養不良につながる危険な老年症候群である．
- 正常嚥下は末梢の感覚神経から大脳皮質までの広い領域の神経系にて精密な制御を受けている．
- 近年，高齢者の遅延した嚥下障害を改善し，誤嚥を予防する抗誤嚥薬がいくつか提唱されている．
- さまざまな嚥下困難に対する対処法と抗誤嚥薬を組み合わせることにより，高齢者の胃瘻などを回避することができうる．

はじめに

嚥下困難は高齢者になるにつれ頻度が増え，肺への誤嚥や栄養不良は嚥下困難の深刻な帰結である．介護上の大きな負担でもあり，不慮の事故による高齢者の死亡原因の1位が窒息であることを考えると，嚥下困難は老年症候群の中でももっとも速やかに対処しなければいけないものの一つである．

嚥下困難は嚥下の機能障害に基づく．その理解のためには正常な嚥下機能の理解が不可欠である．嚥下は食塊や液体を口から胃へ送る協調運動反応である．嚥下は主として3相から構成される．食物が食塊となる口腔相に始まり，食塊を食道に送る咽頭相がそれに続く．各相の嚥下とも末梢の感覚神経から大脳皮質までの広い領域の神経系にて精密な制御を受けている．

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嚥下の皮質性調節機構

これまでの嚥下の中枢神経制御は，嚥下反射の中枢のある延髄を中心に考えられてきたが，近年になって嚥下の大脳皮質による神経調節機構について盛んに研究され，さまざまな知見が得られてきた．PETやfunctional MRIなどの研究から，考えてみれば当然ではあるがFig. 1に示すように，嚥下時には大脳皮質の一次体性感覚野，島皮質，前帯状回といった感覚に関わる領域と，一次運動野，補足運動野，帯状回運動野といった運動に関わる領域の両方が活性化されることがわかってきた[1]．さらにその中で加齢によって活性が障害されるのは感覚に関わる領域であり，運動に関わる領域はその機能が維持されているがゆえに嚥下時に大きな努力が強いられ，高齢者の嚥下時にはその活性が強まっていることが判明した．また，認知症やラクナ脳梗塞などで著明に障害されやすいのも感覚に関わる領域であることがわかってき

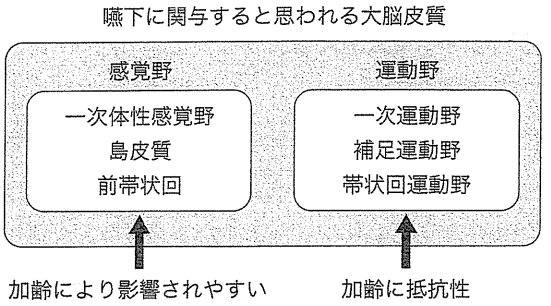

Fig. 1. 嚥下時に活性化される脳部位と加齢の影響

た[1]．また，誤嚥性肺炎患者においてもこれらの領域の脳血流が低下していることもわかった[2]．したがって，嚥下に関わる大脳皮質感覚神経領域を活性化することが，認知症や脳梗塞における嚥下障害において重要であることがわかる．

嚥下機能評価の方法

嚥下機能評価の簡単な方法としては，反復唾液嚥下テスト(repetitive saliva swallowing test：RSST)，改訂水飲みテスト(modified water swallowing test：MWST)，食物テスト(food test：FT)がよく使用される．RSSTは比較的状態がわるい患者にも行え，呼吸状態が安定している場合には水や食物を利用したMWSTやFTが有用な評価法である．また，不顕性誤嚥の評価法としては嚥下反射測定，咳嗽反射の測定などがある．さらに詳しい検査として嚥下造影検査，鼻腔咽喉頭ファイバー検査がある．

1．RSST

検者は指腹を患者の喉頭隆起に置き，唾を実際に嚥下するよう命じ，嚥下運動を観察する．患者に空嚥下(唾液嚥下)を反復してもらい，嚥下反射の随意的な惹起能力を評価する．口腔乾燥のある場合は人工唾液などで口腔を湿潤させてから空嚥下を行ってもらう．高齢者では30秒間に3回以上，空嚥下の反復ができることが正常の目安となり，2回以下であると誤嚥をしている者が多い．空嚥下の評価は嚥下とともに喉頭がしっかり挙上運動することで判断する．

2．MWST

3 m*l* の冷水を口腔内に入れて嚥下を行わせ，嚥下反射誘発の有無，むせ，呼吸の変化を評価する．頸部聴診法を併用すると本検査の判定をより正確に行うことができる．

3．FT

プリンあるいは粥4 gを口腔内に入れ，MWSTと同様に嚥下反射誘発の有無，むせ，呼吸の変化を評価する．本検査も頸部聴診法との併用で判定をより正確に行うことができる．

4．嚥下反射測定

蒸留水(1 cc)を口蓋垂の高さまで挿入した経鼻カテーテル(8 Fr)より注入し，蒸留水注入から嚥下運動が起こるまでの時間を嚥下反射の潜時として測定する．潜時が5秒以上かかるときは嚥下反射が遅延して夜間の不顕性誤嚥が存在している可能性が高い．

5．咳嗽反射測定

刺激物をネブライザーより噴霧し，吸入させて咳嗽反射を誘発させる方法である．刺激物としてカプサイシンやクエン酸を使用するのが一般的である．誤嚥の有無の判別ではなく，気道防御反射の有無をみている．クエン酸法では最低5回咳が出るまで，0.03% から 36% まで増加させる．4.5% のクエン酸でも咳が出なければ咳嗽反射が低下している可能性が高い．

嚥下障害への対処

前述の検査にて嚥下機能の低下が認められた場合には，嚥下性肺炎のリスクがあると考えられる．対処としてはまず嚥下障害を引き起こしている原因・基礎疾患を検索し，できるだけそれに対処する．嚥下訓練，体位，食事法，代償的栄養法，歯科的管理などがあり，さらに必要に応じて手術的対応がある[3]．嚥下障害食として適切な性質は，①味：はっきりと強めの香り，②温度：はっきりと，③きめ：ゼリーのきめが最良，④食塊形成：くずれにくいもの，水溶液と固形物の混合は避けるなどである．増粘剤などの使用が有効である．

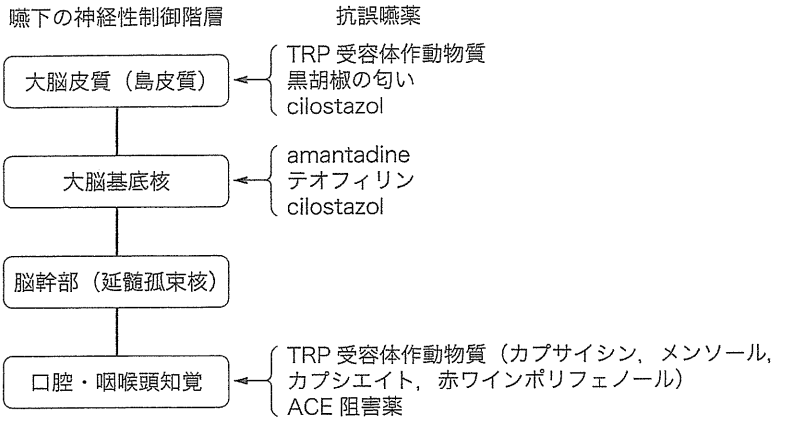

Fig. 2. 嚥下の神経調節の階層性と各種抗誤嚥薬の作用部位

体位では嚥下時はリクライニング位が安全な嚥下において有効であるが，食事後も少なくとも30°以上の座位を保つことが逆流防止上重要である．左右差がある場合は頸部患側回旋が誤嚥しにくい．嚥下訓練については，嚥下は嚥下運動によってもっともよく訓練できる．嚥下反射惹起性が低下し嚥下中誤嚥を伴う患者では，thermal stimulation などにより嚥下惹起の促進を行う．さらに嚥下呼吸強調性を強化し安全性の高い嚥下様式を身につけさせるようにする．

これらの方法に加え，近年さまざまな抗誤嚥薬が提唱されている．それらを嚥下障害患者に投与すると効果がある場合もある．

抗誤嚥薬

近年の老年医学研究の進歩からさまざまな抗誤嚥薬と呼べるものが登場している．先に述べたように嚥下の神経制御は末梢の知覚神経から大脳皮質まで末梢中枢神経全体で制御されている．嚥下の神経性制御の階層性と，それぞれの抗誤嚥薬の作用部位を Fig. 2 に示す．現在のところさまざまな作用部位，作用機序の抗誤嚥薬が提唱されているのがわかる．それぞれについて概説する．

1．温度感受性 TRP 受容体作動薬

高齢者の嚥下反射はたとえ障害されていたとしても，ある程度温度感受性があることが知られている[4]．つまり，体温より離れた温度の食物や水分のほうが飲み込みやすいのである．ヒトが温度を感知する仕組みとして，知覚神経上に温度感受性受容体である TRP 受容体の活性化が関与していることが分子生物学の進歩により判明した．そこでこれらの温度感受性 TRP 受容体を活性化することが温度刺激と同じように高齢者の遅延した嚥下反射を改善することが実証されてきた[5]．高い温度の受容体である TRPV1 のアゴニストであるカプサイシン，カプシエイトが用量依存性に高齢者の嚥下反射を改善することが報告され，さらに TRPV1 のモジュレータである赤ワインポリフェノールも用量依存性に嚥下反射を改善することがわかった[3]．また，冷たいほうの温度の受容体である TRPM8 のアゴニストであるメンソールも用量依存性に嚥下反射を改善することがわかった．さらにこれらの TRP 受容体作動薬は知覚神経に直接的に作用するだけでなく，慢性的に嚥下の皮質制御に重要な島皮質を活性化することにより，嚥下を改善する可能性も示唆されている．

2．黒胡椒精油

黒胡椒精油の匂い刺激は嚥下の皮質制御に重要な島皮質を活性化することにより，嚥下反射を改善する[6]．また嚥下の神経伝達物質として重要なサブスタンス P も増加する作用をもつ．この匂い刺激による治療法アロマセラピーは非常に重度の嚥下障害，意識レベルや ADL の低い高齢者にも行うことができ適応範囲が広い有望な方法である．

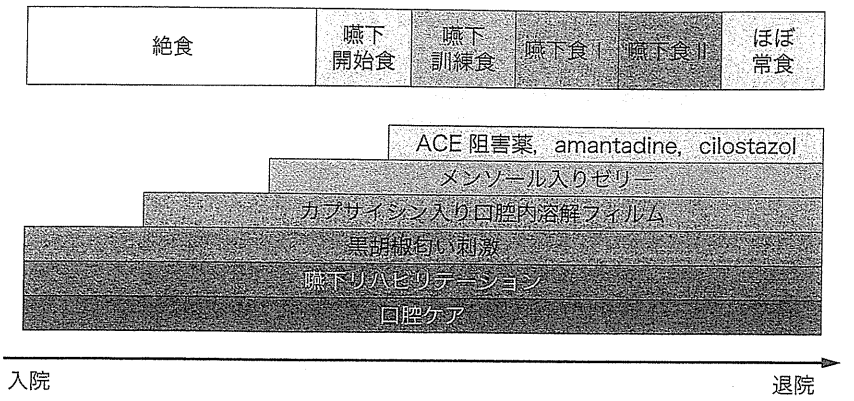

Fig. 3.　誤嚥性肺炎患者の食止めから食事を再開するときのプロトコール

3．cilostazol

ホスホジエステラーゼⅢ阻害薬である cilostazol は抗血小板薬であるとともに脳血流を増やすことが知られ，脳梗塞の治療によく用いられる．cilostazol はサブスタンス P を増加させるとともに，嚥下反射を改善することが知られている[7]．また，継続投与により高齢者の誤嚥性肺炎を予防することができることが報告されている．

4．amantadine

ドーパミンの遊離促進作用をもつ amantadine はおそらく大脳基底核においてその作用を発揮することにより，下位の嚥下反射に関わる神経を活性化し，嚥下反射を改善すると考えられている．長期投与により肺炎の発症を抑えている報告もある[8]．

5．テオフィリン

気管支拡張薬であるテオフィリンはそれより低い濃度で，抑制性神経伝達物質であるアデノシンがその A2 受容体につくのを阻害する．A2 受容体はドーパミン作動性神経上に存在していることが多く，テオフィリンはこの阻害作用によりドーパミン神経の脱抑制を引き起こし，基底核などのドーパミン神経を活性化し，嚥下反射を改善すると考えられている[9]．

6．ACE 阻害薬

降圧薬である ACE 阻害薬はアンジオテンシン変換酵素を阻害する．アンジオテンシン変換酵素はアンジオテンシンⅠの切断のみならず，類似ペプチドであるサブスタンス P も切断する．したがって，ACE 阻害薬は活性体アンジオテンシンⅡの生成を阻害するだけでなく，サブスタンス P の分解を防ぎ，サブスタンス P の活性を上げることとなる．末梢知覚神経においてサブスタンス P は嚥下反射の神経伝達物質なので嚥下反射を改善する結果となる[10]．

誤嚥性肺炎患者の経口摂取開始プロトコール◎

重症の誤嚥性肺炎の患者が入院したときは基本的に絶食である．抗生物質などの治療により患者が回復したとき，食事を開始する過程が実は誤嚥性肺炎の治療においてもっとも重要でかつチャレンジングなステップである．そこで安易に無策に食事を開始したときに再誤嚥となり，それを繰り返すことにより耐性菌が発生したり，衰弱したりして経口摂取を諦めるようになり，胃瘻となったりする．胃瘻をつくったからといって誤嚥性肺炎が防げるわけではない．そこでわれわれはこれまでの原始感覚刺激による高齢者の嚥下機能回復法を集結した，Fig. 3 に示すような誤嚥性肺炎患者の食事開始プロトコールを立案した．重症の誤嚥性肺炎の患者が入院後，点滴治療により回復し，食事を開始するときにこのプロトコールを採用することにより，当病棟では食事再開後の再誤嚥性肺炎の発症が 1/3 に減少したのである[5]．

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認知症の重症化に伴う医学的諸問題　各論

摂食・嚥下障害

Dysphagia in dementia

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Key words：摂食・嚥下障害，食事のクオリア，温度感受性受容体，アロマセラピー

はじめに

認知症高齢者の臨床経過を追跡調査した論文がNew England Journal of Medicineに掲載された[1]．それによると18カ月のフォローアップで86％の人に摂食・嚥下障害が生じ，53％に熱発があり，41％に肺炎のエピソードがあることがわかった．この経過をみると，ここで起こっている肺炎は誤嚥性肺炎であることがうかがえる．以上のことより，摂食・嚥下障害は認知症高齢者の臨床経過においてほぼ必発であり，そしてそれが致死性の誤嚥性肺炎に繋がっていることがわかる．したがって認知症患者の対処において摂食・嚥下障害対策は極めて重要である．

1. 認知症の摂食・嚥下障害

岡田らは認知症高齢者の摂食・嚥下障害の問題点を，①食思の問題，②嗜好の問題，③食物認知の問題，④拙劣な摂食動作の問題，⑤咀嚼から嚥下運動の問題の5項目に大きく分類して認知症患者を調査した[2]．食思の問題が一番多く，食思の低下，過剰な食欲といった問題を起こしている．つぎに単調な咀嚼運動，咀嚼から嚥下への移行困難，呼吸パターンの異常，呼吸機能の低下といった咀嚼から嚥下運動の問題，更に摂取スピードの異常，拙劣な捕食動作といった拙劣な摂食動作の問題が続いた．そして嗜好の問題，食物認知の問題がほぼ同数で続いている．以上のことから考えると認知症患者の摂食・嚥下障害は，脳の高次な情報処理機能の低下によって食事の‘クオリア(感覚質)’を感じ取ることができなくなったことに起因していると思われる．つまり食のクオリアを形成する様々な感覚情報を適切に感じ取り処理することができなくなっているのである．

2. 食事のクオリア

考えてみれば食事は様々な感覚情報から形成されており，それぞれが食事のクオリアの構成要素となっている．それを**図1**にまとめた．まず，最初に思いつくのは味である．それにコク，匂いが加わり風味が形成され，その上にテクスチャー，温度，色・光沢，音が加わり美味しい食事メニューができあがる．しかし，美味しい食事の要素は食べ物そのものの要素だけではない．同じ食べ物でも一緒に食べる人によって美味しくも不味くもなるし，また食事中の楽しい会話は絶好のスパイスでもある．食事に臨む自分の心身状況など，食べ物以外の要素の役割も大きいことがわかる．

この数多くの食事の要素の中で，嚥下食として工夫がされているのは，テクスチャーの要素

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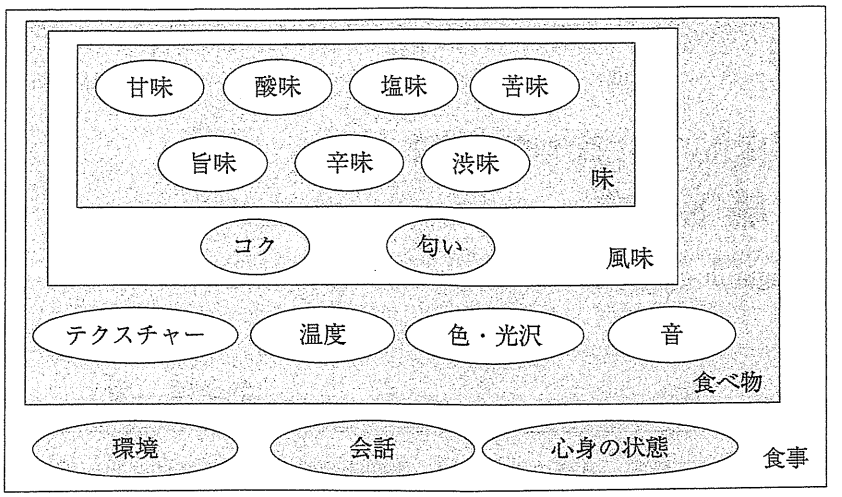

図1 食事のクオリアの要素（文献[3]より改変）

だけである．しかしながら，その他のすべての要素に関して嚥下障害者の嚥下に適したチューニングの方法があると思われ，これまでの嚥下食の効果を考えるとぜひそうすべきである．

3. 温度感覚刺激

著者らが最初にチューニングを考えたのが温度である．つまり嚥下障害をもつ高齢者にとって最も嚥下のしやすい食べ物の温度は何度であろうか，ということである．嚥下障害があり嚥下反射が遅延している高齢者に，様々の温度の蒸留水（1cc）を口蓋垂の高さまで挿入した経鼻カテーテルより注入し，蒸留水注入から嚥下運動が起こるまでの時間を嚥下反射の潜時として測定し，注入した蒸留水の温度と潜時との関係を模式化すると**図2**のようにベル形となった[3]．体温付近において最も嚥下反射が遅延し，温度がそれから離れれば離れるほど嚥下反射の潜時が短縮したのである（**図2**）．本結果は，高齢者の食事は熱いもの，冷たいものの方が嚥下を改善するということを示している．

4. 温度感受性受容体と香辛料

外界の温度受容は，末梢感覚神経が温度刺激を電気信号に変換してその情報が中枢へと伝達されると考えられているが，温度受容にかかわる分子として，哺乳類では末梢神経上に6つのTRP受容体；TRPV1，TRPV2，TRPV3，TRPV4，TRPM8，TRPA1が知られており，それぞれに活性化温度閾値が存在する（TRPV1＞43℃，TRPV2＞52℃，TRPV3＞32–39℃，TRPV4＞27–35℃，TRPM8＜25–28℃，TRPA1＜17℃）．**図2**の下部に示されるように嚥下反射を活性化する温度領域よりこれまで同定されている6個の温度感受性TRPチャネルのうち，TRPV1，TRPV2，TRPM8，TRPA1が嚥下反射の活性化に関与する可能性が示唆された．

実は**図2**の最下部に示されているように，これらの温度感受性受容体には自然界の食品，とりわけ香辛料の中にそのアゴニストが存在するのである．このことが著者らの様々な嚥下障害改善法の開発につながった．

5. 温度感受性受容体刺激による嚥下障害改善法

温度と嚥下反射の関係は，嚥下障害者の食事として温度に変化をつけて食事を出すことの重要性が示唆されている．食事は食べる直前に料理し，できたてのほやほやを食べるようにした方がいいと考えられる．確かにそうではあるが，実際に介護の場面では大変な手間がかかり，現実的ではない場合がある．

そこで著者らは，TRPV1に急性刺激を与えることにより一過性に嚥下反射が改善することや，またTRPV1を慢性的に刺激することにより嚥下反射が持続的に改善されることを示して