

REFLEX RESPONSES TO STIMULATION OF THE UPPER RESPIRATORY TRACT

Z. TOMORI, K. JAVORKA and A. STRÁNSKY

Department of Physiology, Faculty of Medicine,
Comenius University, Martin, Czechoslovakia

Many respiratory, cardiovascular and other reflex effects can be elicited from the nose and the pharynx, but surprisingly they have been little studied. The most important protective reflex from the upper respiratory tract is the apnoeic reflex evoked by intranasal insufflation of irritants such as smoke in laboratory animals and man (Kratschmer 1870, Magne et al. 1925, Allen 1929). The physiological role of this reflex is protection of the respiratory apparatus from penetration and harmful effects of irritants. There is a similar submersion apnoea (the so-called diving reflex) with profound depression of both respiration and the cardiovascular system in aquatic mammals, frogs and birds (Widdicombe 1964). Similar inhibition of respiration and heart rate, together with hypertension, can be elicited by cold liquid or gases applied to the upper respiratory tract or to the facial skin (Ebbecke 1943, Ebbecke and Knüchel 1943, Rall et al. 1945).

Figure 1 A shows the four classical components of Kratschmer's apnoeic reflex elicited by insufflation of xylol vapour into the nose in the anaesthetized rabbit. The blood pressure record shows bradycardia and systemic hypertension. The pleural pressure record and the electromyogram of the diaphragm show apnoea in the end-expiratory position. Photoelectric recording of the glottal lumen demonstrates closure of the glottis which is stronger than during eupnoeic expiration. Further components of this reflex are bronchoconstriction (Dixon and Brodie 1903, Rall et al. 1945, Nadel and Comroe 1961, Nadel and Widdicombe 1962)

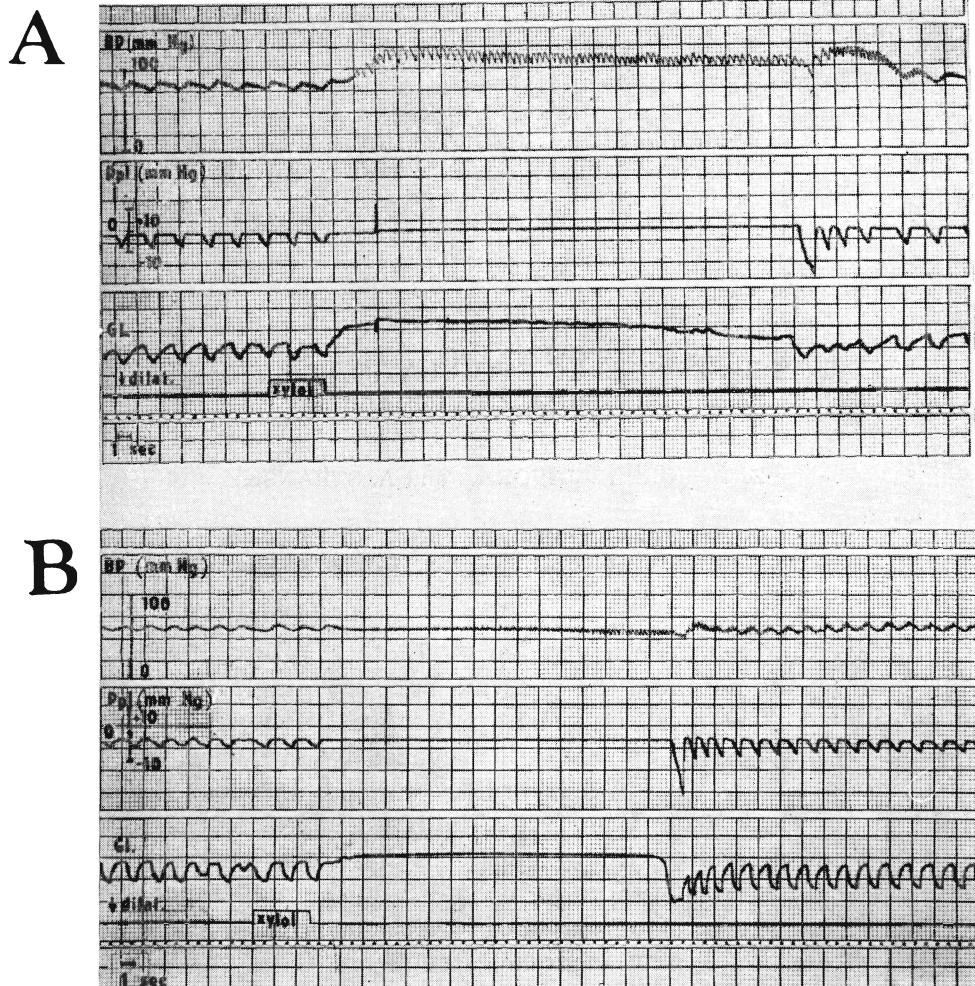


Fig. 1. Cardiovascular, respiratory and glottal changes in apnoeic reflex of nasal origin before (A) and after (B) injection of phenoxybenzamine (2 mg/kg i.v.) in an anaesthetized rabbit. Records from above down: arterial blood pressure (BP), intrapleural pressure (P_{pl}), glottal photopenetration (GL) with dilation downward, signal for nasal insufflation of xylol vapours (xylol) and time in seconds.

and inhibition of skeletal muscle tone (Frankenhaeuser and Lundervold 1949, Andersen 1954). Experiments in anaesthetized rabbits and cats show that the expiratory apnoea elicited by nasal insufflation of irritants is characterized also by strong activity in the expiratory muscles (Fig. 2).

From among the different olfactory and trigeminal stimulations intranasal insufflation of xylol vapour produces the most pronounced cardiovascular, respiratory and glottal effects, and the rabbit proves to be

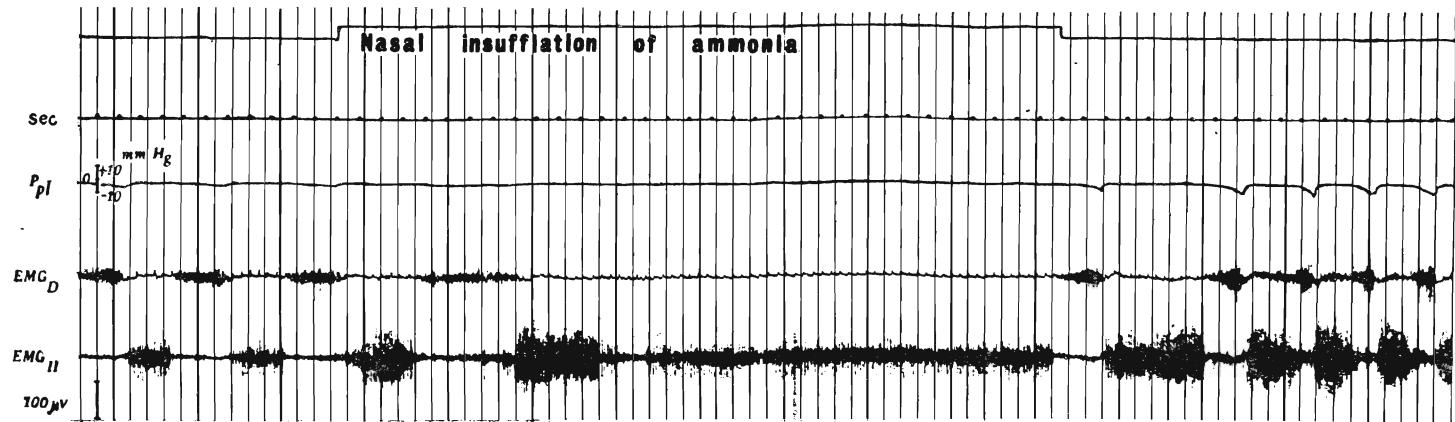


Fig. 2. Changes in intrapleural pressure (P_{pi}) and in the electromyographic activity in the diaphragm (EMG_D), and internal intercostal muscle (EMG_{II}) during nasal insufflation of ammonia. Time in seconds.

the best experimental species for the study of different components of the apnoeic reflex (Tomori et al. 1971). Comparative studies in different mammalian species show that rabbits have the strongest Hering-Breuer inflation reflex too (Widdicombe 1961).

In an effort to suppress some of the components of the apnoeic reflex various types of adrenergic and cholinergic blockade have been used. After intravenous injection of 2 mg/kg of phenoxybenzamine (a potent α -receptor blocker), intranasal insufflation of xylol evokes apnoea and closure of the glottis but the hypertensive reaction is not present as the drug prevents systemic vasoconstriction (Fig. 1B). It is interesting that in anaesthetized rabbits the bradycardia caused by intranasal xylol is also blocked by the drug. In ducks on the other hand the diving reflex bradycardia is not abolished by sympatholytic drugs (Kobinger and Oda 1969). Similar blockade of both the apnoeic hypertension and the bradycardia can be produced in rabbits by other adrenergic blocking substances such as dihydroergotoxine methansulphate (0.3 mg/kg, i.v.) and guanethidine sulphate (3 mg/kg, i.v.). Therefore the apnoeic bradycardia elicited by xylol insufflation in anaesthetized rabbits may be a secondary reaction to hypertension.

Cholinergic blockade produced by vagotomy or by intravenous injection of atropine changes mainly the intensity of the apnoeic and bradycardic components of the reflex elicited by intranasal insufflation of xylol. The duration of apnoea (Fig. 3) is increased by unilateral and even more by bilateral cervical vagotomy as a result of removal of the tonic influence of vagal afferent nerves on the respiratory centre. Similarly vagotomy causes a decrease of respiratory centre reactivity to CO_2 (Guz and Widdicombe 1969). Atropine (1 and 4 mg/kg i.v.) on the other hand decreases the duration of apnoea probably by some central action. The apnoeic bradycardia (Fig. 4) is virtually blocked by bilateral cervical vagotomy, halved by atropine and not influenced by unilateral vagotomy.

It is well-known that reflex apnoea can be elicited in many other ways, e.g., by lung inflation. Figure 5 shows that in anaesthetized rabbits inflation of the lungs evokes not only apnoea and hypotension but also bradycardia and strong closure of the glottis. Electromyographic observations in anaesthetized cats (Fig. 6) reveal that during the inflation apnoea there is strong activity in some laryngeal muscles such as the cricothyroid, as well as in the expiratory intercostal muscles.

One of the most important defensive reflexes from the upper respiratory tract is sneezing, which eliminates the irritants from the nose (like the cough reflex from the lower respiratory tract) by intensive expiratory efforts. The reflex arc, the mechanism and the physiological role of this reflex are discussed in many papers (Sandmann 1887, Bárány

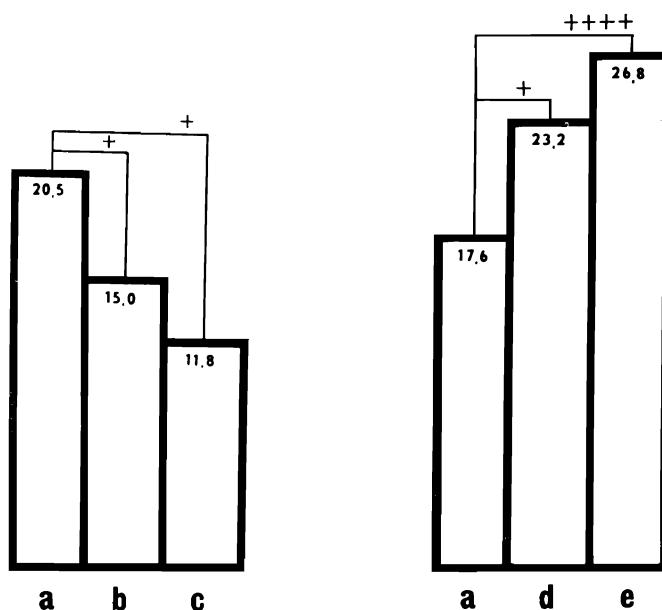


Fig. 3. Duration of the nasal apnoea in control conditions (a), after 1 mg/kg of atropine (b), 4 mg/kg of atropine (c), unilateral (d) and bilateral cervical vagotomy (e). Numbers in the diagrams represent mean values in seconds from groups of anaesthetized rabbits. Significant differences: +, $p < 0.05$ and +++, $p < 0.001$.

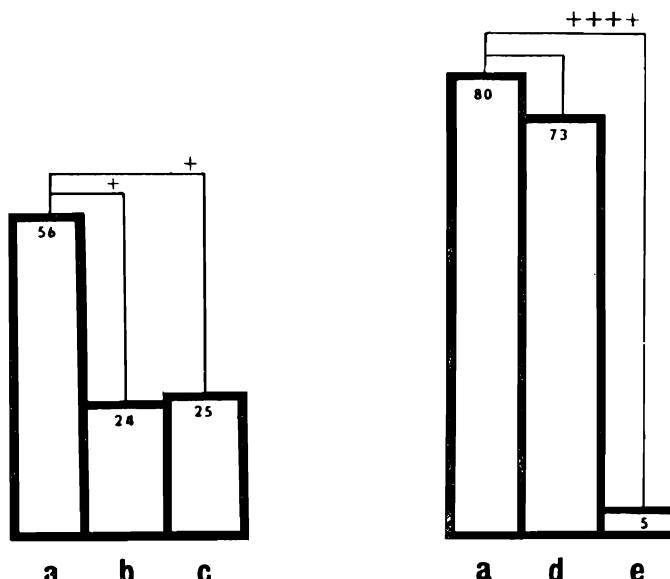


Fig. 4. Apnoeic bradycardia in control conditions (a), after 1 mg/kg of atropine (b), 4 mg/kg of atropine (c), unilateral (d) and bilateral cervical vagotomy (e). Numbers in the diagrams are mean values from groups of anaesthetized rabbits. Significant differences: +, $p < 0.05$ and +++, $p < 0.001$.

1913, Brubaker 1919, Bucher 1952, Massion et al. 1954, Birck 1959, Burkart and Bucher 1960, Tomori 1965).

Instead of apnoeic and sneezing reflexes in experimental animals, there have occasionally been seen fast and deep sniff-like inspirations on intranasal insufflation of olfactory irritants (Beyer 1901, Allen 1936). Sniffing — drawing air through the nose by short inhalations — is a respiratory pattern accompanying the act of smelling or an act (or



Fig. 5. Cardiovascular, respiratory, glottal and electromyographic changes elicited by lung inflation with air (50 ml). Records as in Fig. 1.

habit) of clearing the nose by a short inhalation. In the first case it is interpreted as a cortical activation of respiration elicited particularly by aromatic and balsam-like substances (Oberholzer and Tofani 1960). During the sniff the odoriferous air by-passes the olfactory area, but during the pause following a sniff air tends to move upward over the olfactory area (Dawes 1952) and makes it possible for "a fleeting scent to be caught and held for identification" (Proctor 1964). In the second case, sniffing is a symptom accompanying inflammations of the upper respiratory tract (such as chronic rhinitis or snuffles, sinusitis, adenoidal vegetations), and helps to remove the pathological materials accumulated in this area.

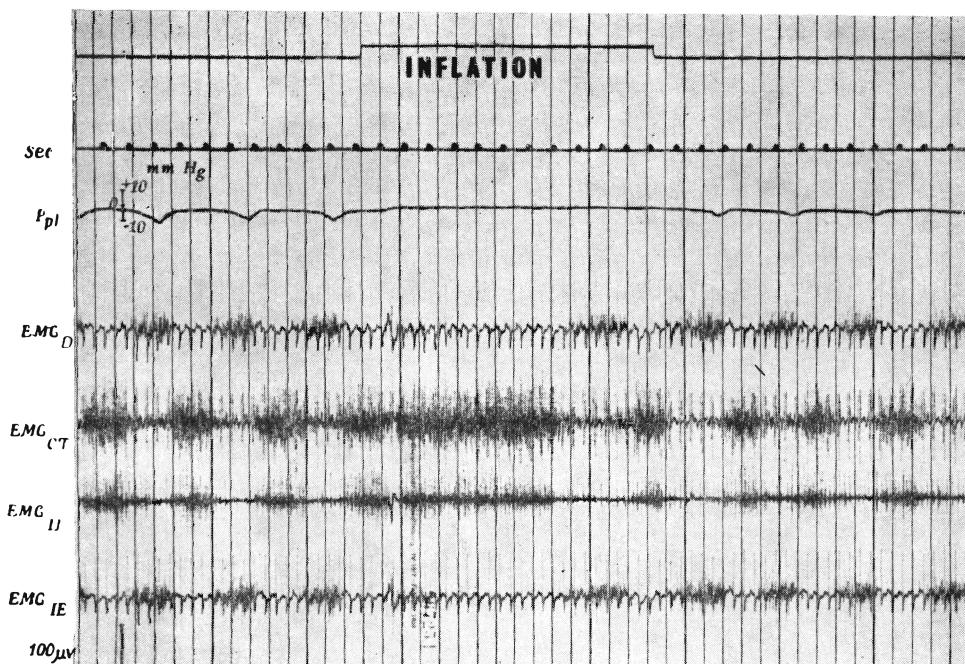


Fig. 6. Electromyographic activity in the diaphragm (EMG_D), cricothyroid muscle (EMG_{CT}), internal intercostal muscle (EMG_{II}) and external intercostal muscle (EMG_{IE}) during inflation apnoea.

There are a few papers describing reflex deepening and acceleration of inspiration by stimulation of the palatine and pharyngeal regions (Teitelbaum and Ries 1934, 1935, Teitelbaum et al. 1936, Takagi et al. 1966), or occasional deep inspirations during mechanical irritation of this area (Sandmann 1887, Burkart 1960, Peñalozo-Rojas and Alcocer-Cuarón 1967). In cats and rats mechanical stimulation of the epipharyngeal (nasopharyngeal) and oropharyngeal mucosae evokes the so-called aspiration reflex comprising sniff- and gasp-like and powerful inspiratory twitches accompanied by reflex hypertension, dilation of the glottis, bronchodilation and strong bursts of activity in efferent sympathetic nerves (Tomori et al. 1957, Tomori 1962, 1965, Tomori and Korec 1964, Tomori and Widdicombe 1969, Korpáš 1970). This aspiration reflex can be easily elicited in anaesthetized cats by intranasal instillation of 0.1–0.4 ml of water (Fig. 7A) or by repetitive contacts of a nylon fibre of 0.5 mm diameter with the epipharyngeal mucosa (Fig. 7B). Gentle introduction and withdrawal of a nasal catheter or slow intranasal insufflation of 100 ml of air have practically no respiratory effects. The aspiration reflex can also be elicited by insufflation of air into the

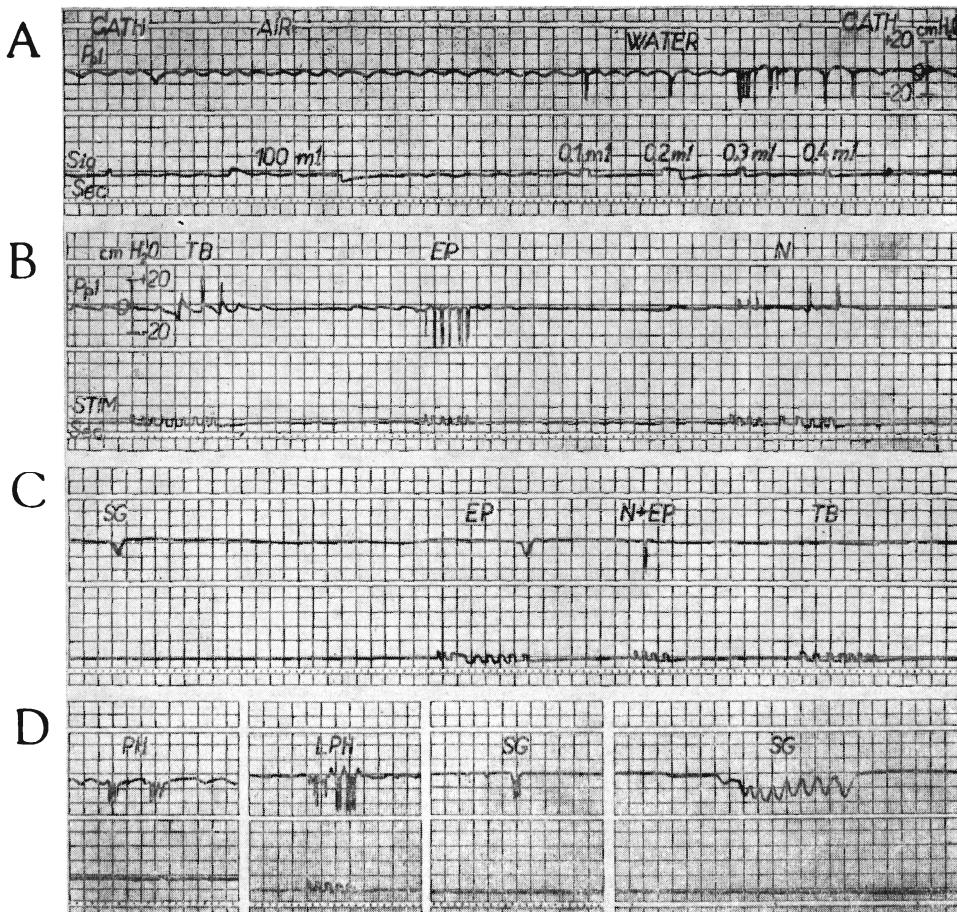


Fig. 7. Respiratory reactions to mechanical stimulation of the nasal (N), epipharyngeal (EP), laryngopharyngeal (LPH) and tracheobronchial (TB) mucosa in anaesthetized cats in control conditions (A and B) and during agony elicited by CO_2 inhalation (C and D). P_{pl} , intrapleural pressure; Cath, introduction or withdrawal of a nasal catheter; Water, nasal instillation of 0.1–0.4 ml water; SG, spontaneous gasps. For description see text.

upper respiratory tract when there is deformation of the mucosa (Nail et al. 1969). The reflex draws the irritants from the nasopharynx to the oropharynx by fast and powerful inspiratory efforts aiding the ciliary transport which is directed towards the orifice of the oesophagus (Proctor 1964). The reflex is present in deep stages of general anaesthesia and also in hypothermia when sneeze, cough, swallowing, corneal and pupillary reflexes are absent (Korpáš and Tomori 1957, Tomori 1968) and therefore may play an important role in the development of tracheobronchial aspiration.

Figure 7 shows an experiment in an anaesthetized cat where, after a control record of sneezing, coughing and the aspiration reflex (Fig. 7B), inhalation of very high concentrations of CO_2 evokes an agony with spontaneous gasps. During this stage mechanical stimulation of the epipharyngeal mucosa evokes reflex gasps (aspiration reflex) while nasal and tracheobronchial irritations have practically no effect. A similar situation occurs immediately after injection of chlorpromazine (5 mg/kg i.v.) when there is no sneeze or cough reaction to nasal or tracheobronchial stimulation; at this time the reactivity to epipharyngeal stimulation remains very high (Tomori 1970).

Figure 8 demonstrates that irritation of the epipharynx is such a strong stimulus that it can immediately interrupt by the aspiration

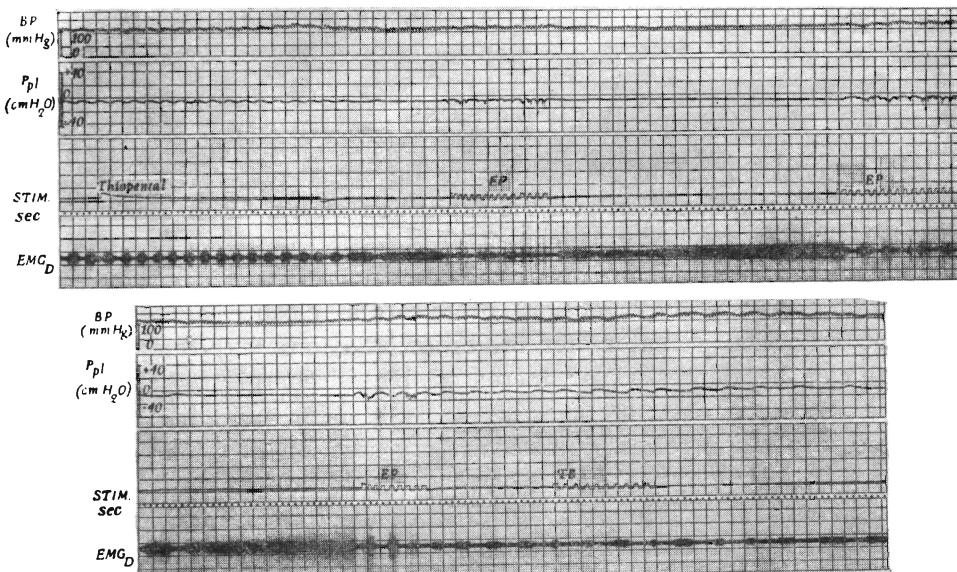


Fig. 8. Interruption of thiopentone apnoea by mechanical stimulation of the epipharynx (EP) in an anaesthetized cat, while tracheobronchial (TB) stimulation is ineffective. Symbols are as in earlier Figures. For description see text.

reflex the apnoea elicited by intravenous injection of sodium thiopentone (20 mg/kg) in a cat already anaesthetized with pentobarbitone (40 mg/kg, i.v.). Similar stimulations of other areas of the respiratory tract are ineffective. Nasopharyngeal stimulation can probably interrupt any respiratory state, and this reflex may play a role in the interruption of hiccough by nasopharyngeal stimulation observed in patients (Salem 1967, Moses et al. 1970). The aspiration reflex may contribute to such processes as sniffing, gasping and retching and it may be involved in

the olfactory nervous discharges of purely mechanical origin described by many authors (Adrian 1942, 1951, Ueki and Domino 1961, Peñalozo-Rojas and Alcocer-Cuarón 1967, Stone et al. 1968, Stone and Rebert 1970).

Because of the simplicity of its production and because of its extraordinary biological strength the aspiration reflex represents a method useful for the study of the mechanisms of such reflex effects as sniffing, gasping, dilation of the glottis, bronchodilation, respiratory arrhythmia and hypertension.

The normal rhythm and depth of breathing is influenced by reflex effects from the upper respiratory tract, the most physiological stimulus being the stream of air (Sergievskii 1950, Bosma 1957, Felberbaum 1963, Widdicombe 1964). In a similar way nasal breathing can be accompanied by thoracic distension lasting a few minutes, a nasothoracic reflex (Sercer 1935).

CONCLUSIONS

1. The most important reflexes from the upper respiratory tract are sneezing, the apnoeic reflex and the aspiration reflex. Their mechanisms are very complex and not yet clear.
2. Some of the components of the apnoeic reflex elicited by nasal stimulation (apnoea, hypertension, bradycardia, closure of the glottis, bronchoconstriction, somatomotor inhibition and tonic expiratory muscle activity) can be depressed or increased by adrenergic or cholinergic blockade.
3. The "aspiration reflex" is a respiratory reaction extremely resistant to suppression by physical and pharmacological influences and it can play an important role in many modifications of breathing, as well as in development of tracheobronchial aspiration.

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Z. TOMORI, K. JAVORKA and A. STRĀNSKY, Department of Physiology, Faculty of Medicine, Comenius University, Muzealna 6, Martin, Czechoslovakia.