### SOME INVESTIGATIONS ON THE FUNCTION OF SMELL

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## Introduction:

Much less is known concerning the nature of the olfactory stimulus, the action of the organ, and the facts inherent in the sensation of smelling, than about the corresponding factors in audition and vision. Among the more recent theories concerning olfaction that of **Bungenberg de Jong** stands out by its simplicity and plausibility. Solutions and coacervates of phosphatides, combined with lipoids, are very sensitive to olfactory molecules, and are both hydrophilic and lyophilic. As these substances are present in the organ of smell, it is reasonable to assume that changes in the structure of these substances constitute the stimulus of the nervous elements.

Of the different olfactometrical methods the most practical and most physiological is to get the testee to sniff up dilutions of smells in rising concentrations. To this end the perfume industry soaks filter paper in the solution. In the Leyden Clinic — following **Proetz** — small flasks are used for this purpose. The blast-injection method of **Elsberg**, being perhaps more accurate, requires a complicated apparatus, the tests being time consuming. The same holds true for the method of **Zwaardemaker**.

We investigated whether it would be better to determine the identification threshold, or the sensation threshold. It was found that the nomenclature of substances — even if the smell is familiar — is to difficult. For this reason the determination of the sensation threshold is more practical. It appeared, however, that the testee's expectation that he is going to smell a known substance, leads to erroneous observations in the case of weak smells. The same applies when it is suggested to him that he will smell, say, camphor, while in reality he is offered petroleum. These observations prove the relative unreliability of a weak sensation and are therefore forensically important. In clinical olfactometry one should offer the patient a smell with which he is familiar, in rising concentrations. When falling concentrations are used, olfactory fatigue soon sets in. In this way, well reproduceable values are obtained.

#### Hyposmia and hyperosmia in adults

In groups of testees selected at random the sensation thresholds were determined for camphor, petroleum and ethanol in different solvents in order to examine the influence of the solvent on the olfactory threshold. The sensation threshold for ethanol in sesame oil was 1 : 100 that of ethanol in glycerin, 1 : 250. As the norm for the sensation threshold of a given substance we took the median, i.e. that concentration which just came within the limits of perception of 50 per cent of the testees. Half of the testees whose threshold was lower than this value were qualified as the better- and the other half as the inferior "smellers". Those in whom the olfactory sensation only appeared at a dilution between 1 : 100 and 1 : 100 were ranked with the inferior smellers;

those who already experienced the sensation at a dilution of from 1 : 2500 to 1 : 3000, constituted the sharp smellers.

The number of experimental subjects was about 700 men and woman between 15 and 80 years. Hyposmia was found as well with men as with woman in  $\pm$  22%. Among the woman sharp smellers were found in 22% against among the men only in 11%. It was found that the number of inferior smellers increased with the testees' ages. Mainly the older testees were aware of their olfactory deficiency: probably for one thing, because in their case hyposmia was more serious than in the younger persons. The difference in smelling sharpness as between men and woman older than 50 was only slight and definitely does not point to smoking as a cause of the decline of olfaction in men. It is certain that allergy is an important factor in the genesis of hyposmia. Pregnancy, on the contrary, is not.

#### Olfactometry and taste in children

Olfactometry in children has its own special difficulties, which can best be solved in a play-situation. Since no method to this end is known as yet, experiments were made for this purpose. The best method appeared to be to fill one flask with peppermints, and two other flasks with tablets without any peppermint odour. The child is then asked to make a choice from these flasks, being guided by his sense of smell. The decisiveness with which a well smelling child makes the right choice is unmistakable. The sense of smell can be studied in this way in children from 2 years of age upwards. In some cases, unilateral or bilateral anosmia was established by this method.

It was found from these experiments that the young child uses his olfactory sensation in order to obtain an agreeable kind of food. It is questionable, however, whether, in the young child, the sense of taste is dominated by the sense of smell to the same extent as in adults. In order to ascertain this, 29 children between 1 and 5 years of age were given ordinary cream puffs, and also cream puffs that had been made disgusting with an injection of asafoetida. It was found that all children older than 4 years of age refused the asafoetida cream puffs, and that, out of 22 children below 4 years of age, only 3 showed a repugnance reaction. Olfactory preference and tasting by smell, therefore, are still underdeveloped in the young child.

### So called "Haematogenous Olfaction"

In common with any other sensory disturbance, so in the case of anosmia, the first thing to ascertain is whether we have to do with a perceptive disorder, or with a disturbance in the transmission of the stimulus to the cells of the sensorium involved. In the case of the organ of smell this involves the problem if the olfactory cleft is open and filled with air or with secretion. The first condition is an absolute necessity in order to smell. Inspection of the clefts is imcomplete and consequently we must rely on tests and the patients own observations.

If a patient experiences occassionally a smell, this proves undoubtely that perception is in tact. We know allergic patients suffering from anosmia who, before a dinner, with corticosteroids, recover their olfaction and taste temporary. Bednar and Langfelder, Marco Clemente and Wesely, and Dussik and Kaunders reasoned that if it would be possible to elicitate a sensation in a patient by direct stimulation of the sensory cells — any existing anosmia must be due to a defective transmission of the inhaled odours. The so called "haematogenous olfaction" was effected by injection of odorous substances as camphor intravenously. This, therefore should be a similar experiment for olfaction as Rinne's experiment for audition.

In order to investigate this important test, we injected intravenously into testees, various quantities of, inter alia, camphor and ether. It was found that, providing the dosis was sufficiently high, the subjects did, in fact, experience an olfactory sensation. In 5 patients with anosmia as a result of ozaena, there was no sensation of smell.

If the experiment is to be valuable, then in case of pure transmission anosmia an intravenous administration of an odour should be followed by an olfactory sensation. In order to ascertain this we introduced water into the olfactory cleft in 5 normal test-subjects, in supine position and in 2 other testees, a rubber condom was introduced into each half of the nose, and inflated. It was found that none of these subjects got any olfactory sensation after the intravenous injection. But, when either the water or the condom was removed relatively quickly, the olfactory sensation did occur. Consequently so called haematogenous olfaction is not a stimulation of the sensory cells by way of the blood stream, but most probably a diffusion of the odour out of the blood into the olfactory cleft or in the lung.

In order to test these two possibilities we found, that with camphor after the intravenous injection the sensation of smell is conditioned by the expiratory air. During the period that a person held his breath, no olfactory sensation occurred. During the first expiration however camphor was smelled.

Patients in whom the larynx had been surgically removed had, despite their normal sense of smell no haematogenic olfactory sensation at all for camphor. However ether injected in the bloodstream was perceived by them. A odorous substance as camphor therefore, must be excreted in the lungs, reaching the olfactory cleft together with the expiratory air whereas the volatile ether proved to pass the capillary vessels of the nose and the olfactory cleft.

## **Expiratory** olfaction

Investigation of patients suffering from inspiratory anosmia showed that some of them nevertheless had a sensation of smell after the intravenous administration of the odorous substance, especially when expiring with force. This proves that the expiratory air-current can still reach the olfactory cleft, even when the inspiratory current cannot. The original conception of Wessely et al. concerning the diagnostic significance of haematogenic smelling as a means to prove that the organ is intact, therefore, has a definite factual foundation. The explanation, however, is not that the central organ has been haematogenically stimulated, but lies in the superiority of expiratory olfaction.

Taste is to a large extent expiratory olfaction. Anosmia patients often have an undisturbed sense of taste, thanks to this superior expiratory smelling. Wine-tasters evaluate the arome of wine by taking a sip and making masticating movements. This too causes the odour to reach the olfactory cleft via the nasopharynx.

On the basis of this observation a method was elaborated to provoke an expiratory olfactory sensation. With the aid of a piece of cottonwool fixed on a small rod a 10 per cent. solution of camphor in liquid paraffin was applied through the mouth to the pharyngeal wall. The patient was then asked whether he got a sensation of smell on breathing out. It was found that the great majority of normal testees had a stronger perception of the olfactory sensation from expiration than from inspiration of the same solution. It is necessary, however, to pay particular attention to the first and the second expiration, as many test subjects appeared to be rapidly subject to olfactory fatigue.

This simple method of testing expiratory olfaction proved to be clinically useful. Whenever a sensation was obtained, then this proved that the patient's organ of smell was intact, which suggested a therapy directed towards the removal of a transmissive disturbance.

# Masking and Fatigue in olfaction

The interaction between scents is an important problem in the perfume industry; it is also however, a hygienic problem in fighting foul smells. Odours may either strengthen or neutralize each other. A strong smell may mask a weak one; and one smell may sooner cause olfactory fatigue than another. We investigated on what principle the action of an active deodorant (Airwick) is founded.

It appeared that the organ of smell is less quickly fatigued by the deodorant than by stench. Since the sensation thresholds of the deodorant and carbon disulphide are equal i.e. 1 : 15000, the two substances are fairly well comparable. We found that, in 5 test subjects, fatigue for carbon disulphide occurred after 19 minutes, and for the deodorant after 30 minutes. In fact from these observations it may be concluded that, even when the stench initially predominates, the deodorant will persist after a short time. This is wrongly called the removal of offensive smells. When a new stench appears in a room pervaded by a deodorant, the observer who has been present inside that space for some time will smell the new stench undiminished, because he already has a degree of fatigue for the deodorant.

Fatigue of one half of the nose need not imply fatigue of the other half. This may be confirmed by simple experiments. If, for instance, one inhales a perfume through one nostril, and expires through the mouth fatigue soon sets in. But on inhaling the perfume through the other nostril one will at once get a fresh strong sensation. In superficial breathing, fatigue will affect part of the olfactory epithelium; deep breathing, or sniffing will again produce a strong smelling sensation.

Thus olfactory fatigue has an — unknown — substratum in the olfactory epithelium and is, therefore a peripheral phenomenon.

### Compensation and neutralisation

Zwaardemaker was the first to study the phenomenon of compensation or neutralisation. If the smells in rising concentrations of our deodorant and carbon disulphide, are mixed, it appeared that the mixture could be nearly odourless, while the separate flasks emitted a strong smell.

If the deodorant and carbon disulphide smells were applied simultanously each to one nostril, it was found that there existed a distinct compensation; so much so that, sometimes, smelling two solutions of 1 : 100 produced no sensation at all. This compensation, therefore, must be a central olfactory inhibition.

The following, extremely notable test — already made by other investigators — shows very clearly that olfactory fatigue acts peripherally and masking centrally. Flask A contains only a deodorant, flask B the deodorant with a trace of carbon disulphide. Both flasks, therefore, strongly smell of the deodorant. Now if one smells at flask A until fatigue for the deodorant sets in, one will find that flask B smells of carbon disulphide. This proves that the initial masking of the carbon disulphide by the deodorant disappears owing to peripheral fatigue. The deodorant stimulus no longer reach the centre. This test shows that neutralization is not a chemical process of elimination of the substances and neither temporary damaging of nervous elements, as the peripheral fatigue of the olfactory epithelium. One smell leaves the epithelium intact for transmitting the stiumulus of another smell.

### **QUELQUES RECHERCHES SUR LA FONCTION OLFACTIVE**

L'olfactométrie selon Proetz est pratiquée avec des dilutions d'odeur en bouteilles que l'on fait humer au malade. L'identification d'une matière étant difficile, l'on doit rechercher le seuil de sensation. Le dissolvant change cette valeur. Parmi 700 sujets de tout âge 22% souffraient d'hyposmie. L'hyperosmie se rencontrait chez l'homme, en 11% et chez la femme en 22% des cas.

Une nouvelle méthode d'olfactométrie chez l'enfant fut introduite, basée sur le choix d'une bouteille avec des pastilles de menthe entre d'autres bouteilles contenant des pastilles neutres.

L'olfaction hématogène, c'est à dire la sensation olfactive provoquée par l'injection intraveneuse d'un produit odorant, pourrait n'être que la sécretion de l'odeur dans les poumons atteignant la fente olfactive avec l'air expiré.

Il se prouvait que cette olfaction expiratoire est souvent supérieure et qu'une anosmie inspiratoire de transmission peut-être décelée en appliquant un produit odorant au pharynx.

La fatigue olfactive est un phénomène périphérique: si l'un côté du nez est fatigué l'autre reste normal. Au contraire le phénomène de masque des odeurs est central: si un côté du nez reçoit une certaine odeur, cette sensation peut-être masquée par une autre odeur administrée de l'autre côté du nez.

### BIBLIOGRAPHY

Versteeg, N.: Onderzoekingen over de reuk. Thesis, Leiden (1956).

Bungenberg de Jong, H. G .: Models for the stimulation of the organ of smell.

Proetz, A. W .: Physiology of the nose. Annals Publishing Company, St. Louis.

Elsberg, Ch. A.: The newer aspects of olfactory Physiology and their diagnostic applications. Archives of Neurology and Psychiatry. Vol. 37, 2 (1937).

Bednar, M. and Langfelder, O.: Über das intravenöse (hämatogene) Riechen. Monatschr. f. Ohrenheilk. 64, 1133–1139, (1930).

Zwaardemaker, H.: L'odorat, Paris, Doin (Encyclopédie scientifique) (1925).

Zwaardemaker, H .: The sense of smell. Acta Oto-Laryng. 2, (1927).

Dishoeck, H. A. E. van and Versteeg, N.: On the problem of Haematogenic olfaction. Acta Oto-Laryng., 47 - 5- (1957).

Hennebert, P. E.: L'Olfaction. Acta. Oto-Rhino-Laryng. belg. 2, Rapp. IV Congress Soc. Belg. Oto-Rhino-Laryng. June (1953).

Marco Clemente and Wessely Dussik and Kaunders See van Dishoeck and Versteeg.

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