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Practical test kits for quantitatively evaluating the sense of smell

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SUMMARY

A set of polypropylene squeeze-bottles, containing serial dilutions of pyridine in mineral oil, are used to deliver puffs of accurately odorized air to the nose. The patient's olfactory threshold can be quantitatively measured in a few minutes, and placed in the normal, hyposmic or hyperosmic range of sensitivity.

INTRODUCTION

Although abnormalities of the sense of smell offer considerable diagnostic value (Van Den Eeckhaut, 1978; Doty, 1979), quantitative olfactory testing is seldom performed in clinical practice. Recently one of us described an accurate test method, utilizing binary-step serial dilutions of pyridine in water (Sherman, Amoore and Weigel, 1979). Nevertheless, the procedure required at least two hours preparation, for cleaning the glass-stoppered flasks and making up the test series. Furthermore, the stronger solutions leak pyridine vapor through the ground-glass surfaces, and the weaker solutions become unreliable after about a week, on account of microbiological activity. Lesser, but still significant, problems are the fragility of the flasks and the tendency of the stoppers to stick. Observant patients may use non-olfactory clues to recognize individual flasks by defects in the glass, or by the increased fingerprinting or noticeable warmth of the common set of blank comparison flasks, caused by their more frequent handling during the test. These disadvantages are virtually eliminated by the new method. The use of plastic squeeze-bottles for olfactory threshold measurements was pioneered by Guadagni et al. (1963). They use 8-oz Teflon bottles with Teflon air delivery tubes inserted through the screw-caps. Amoore and Buttery (1978) demonstrated that both the glass-flask and the squeeze-bottle methods yield exactly the same threshold, when the vessels contain the same concentration of odorant in solution. Various oils are odorless and stable solvents for odorous compounds, and have been used for research on olfactory sensitivity. In the case of the musk pentadecalactone, whose aqueous solutions decompose in a few hours, the

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dilutions in mineral oil retain their potency for several months (Kalmus and Seedburgh, 1975). These considerations suggest that a really practical clinical olfactory test method could be based on mineral oil solutions of pyridine in plastic squeeze-bottles.

METHODS

Among various plastics and bottles tested, the most suitable are odorless white polypropylene 8-oz (250 ml) cylindrical squeeze-bottles, of the type commonly used for shampoo. The bottle caps incorporate flip-top spouts (orifice 2.5 mm diameter) that are opened by pressing on one side, and closed by pushing on the other. These bottles are vapor-tight, unbreakable (above 0°C) and resistant to creasing when squeezed repeatedly. The opaque white pigment conceals the contents, reduces light penetration, and does not show fingerprints. Each bottle contains 2-oz (60 ml) of odorless light mineral oil (White Oil, U.S. Pharmacopoeia grade) of viscosity about 85 Saybolt seconds at 38°C. The oil in each odor test bottle contains a measured concentration of pyridine (C_5H_5N, analytical reagent grade). The air in the bottle promptly acquires (within 30 seconds) the equilibrium concentration of pyridine vapor, which has a characteristic odor, reminiscent of scallops.

Each successive binary step of the dilution scale contains pyridine at one-half the concentration of the preceding step. The dilution series of pyridine solutions in mineral oil is designed to match the odor intensities of the standardized scale of pyridine solutions in water described by Sherman et al. (1979). It transpired that the air/oil partition coefficent for pyridine is approximately one-half of the air/water partition coefficient. Accordingly, the concentration of pyridine for the equivalent intensity binary dilution step has to be doubled in the mineral oil series. The concentration of odorant vapor in the air-space at equilibrium is directly proportional to the odorant concentration in the solution, up to at least 1% solution, in conformity with Henry's Law (see discussion by Amoore and Buttery, 1978).

Each pyridine odor bottle is accompanied by its own matching blank bottle, identical in all respects except for the absence of pyridine from its mineral oil. Paired blank bottles are necessary for proving that the patient can positively distinguish the odor. The use of dedicated blank bottles ensures that the odor-test and blank bottles receive the same amount of handling and ventilation. Bottles are identified by pressure-sensitive lables applied under the base, where they cannot be seen by patient or tester, until after the patient's choice has been made (raise the bottle above eye level to read the label). The appropriate set of squeeze-bottles is kept in a labeled carton, at room temperature (Figure 1). Binary steps no. 6 through 29 of the pyridine scale (Sherman et al., 1979) have been found adequate to cover the maximum range ordinarily required in clinical practice. (Ready-to-

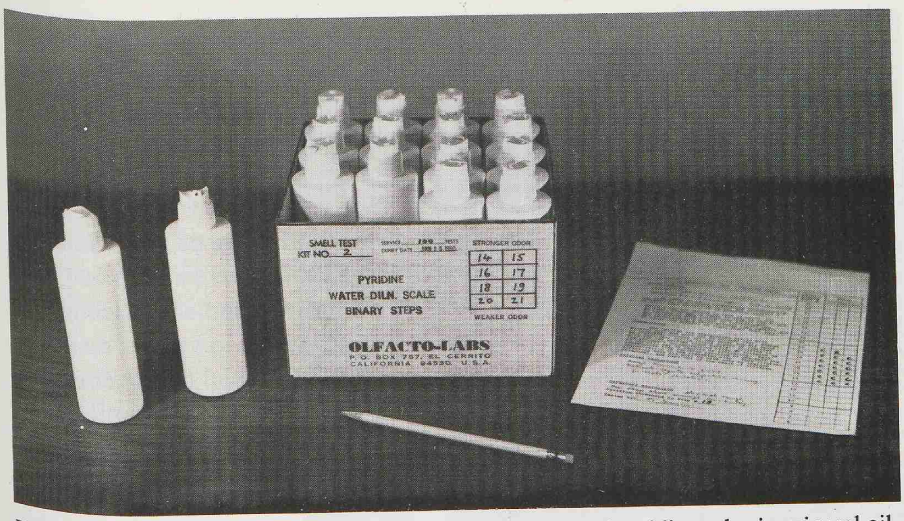

Figure 1. Clinical smell test kit, providing serial dilutions of pyridine odor in mineral oil.

use test kits, in a variety of sensitivity ranges to suit particular applications, were introduced commercially in 1979, and are available from Olfacto-Labs, P.O. Box 757, El Cerrito, California 94530, U.S.A.)

RESULTS

To obtain the most reliable result, and to avoid contaminating the bottles, the patient should not have smoked or eaten during the preceding 15 minutes, or used any perfumed cosmetics that day. A cold, influenza or mild nasal allergy may reduce sensitivity about two steps. Before each test, the selected pair of bottles should be swirled to hasten equilibration between the liquid and the vapor in the air-space, then the orifices are flipped open. The patient is instructed to direct the orifice closely toward the nostrils, then to squeeze the bottle while inhaling through the nose (Figure 2). The patient has to pick out the odorous, or most odorous, bottle of the pair. Unless the odor is very obvious, the test should be performed three times at each sensitivity step; the bottles being swirled and randomized, out of sight of the patient, before each test. In this way, misleading results due to lucky guessing by the patient can be avoided. It is convenient to start with binary step 14, and then use weaker, or stronger, odor intensities as required to determine the patient's olfactory detection threshold for pyridine. The threshold is defined as the weakest odor step at which the patient selects the correct bottle all three times. Less than ten minutes are required for questioning and testing each patient.

Olfactory thresholds determined with the mineral oil dilutions of pyridine are virtually identical to those described by Sherman et al. (1979) for aqueous pyridine

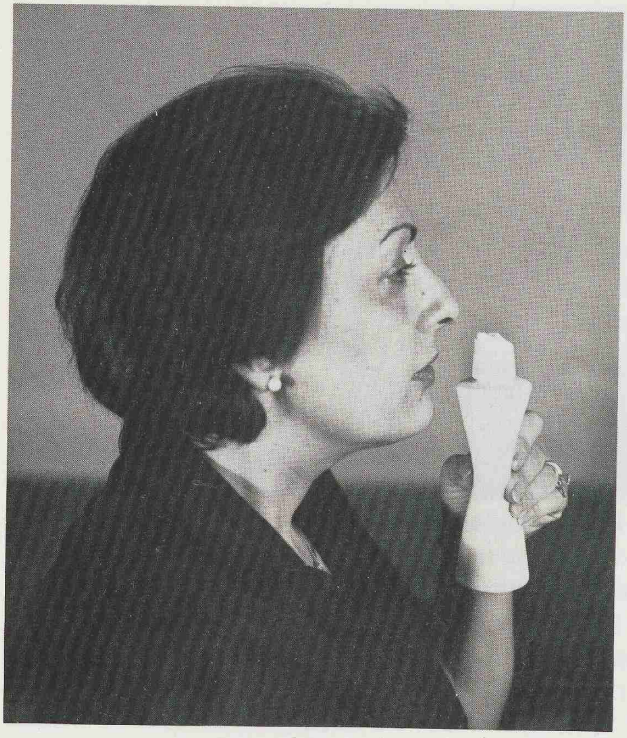

Figure 2.
The patient squeezes the test bottle, to direct the odorized air toward the nostrils.

dilutions. The normal range of sensitivities (96% of healthy persons aged 20–60 years) lies from step 14 to step 21, with the mean sensitivity at step 18.0 (standard deviation ± 2.0 steps). The reproducibility of the test on the same person, in good health but on different occasions, is ± 1 step. Any patient who cannot distinguish step 10 pyridine is considered to have no olfactory (1st cranial) nerve sensitivity. This condition, hyposmia type I in Henkin's (1967) terminology, has been observed in a variety of pathological conditions. Such patients may nevertheless be able to detect pyridine vapor at step 9 or lower sensitivity, by means of irritant, tingling sensations from the trigeminal (5th cranial) and other nerves in the nose and pharynx (9th and 10th cranial). Threshold sensitivities in the range of step 10 through step 13 represent hyposmia type II (Henkin, 1967), and are often associated with clinical abnormalities. An ability to detect pyridine at step 22 and greater sensitivities represents hyperosmia, and may also be indicative of a clinical condition.

DISCUSSION

The pyridine solutions in mineral oil show no sign of microbial or chemical deterioration even after 12 months. The anhydrous nature of the diluent, and the pres-

ence of an anti-oxidant (tocopherols) in the mineral oil, probably contribute to this stability. There is a barely detectable permeation of pyridine through the plastic walls of the bottles. This loss amounts to much less than one binary step of sensitivity in 12 months. More significant is the discharge of pyridine vapor each time the test is performed. Each squeeze of the bottle delivers a volume of air about equal to the volume of mineral oil (60 ml). The partition coefficient for pyridine between air and mineral oil is approximately 1 : 3,400 on a weight/volume basis. Hence each squeeze of the bottle removes 1/3,400 part of the pyridine remaining in the bottle. It may be calculated that, if each patient squeezes the bottle an average of three times in each of the three tests at a given binary step, 200 patients can be put through the threshold determination, before the bottle would lose one binary step of pyridine concentration.

A disadvantage in this test method is that the squeeze bottles must not be knocked over, shaken or inverted, because oil may enter the air delivery orifice. If this happens, the dispenser cap should be removed and cleaned out with facial tissue. The pyridine itself in the higher concentrations is an irritant, as indeed it has to be in order to act as a trigeminal nerve stimulant. For these reasons the test should only be administered by personnel who have been well instructed in its use. The mineral oil, and the polypropylene plastic, may develop detectable background odors after 12 months. Therefore it is advisable to discard and replace the kit annually, even though it may not have been employed to its rated service limit of 200 thereshold tests. To the best of our belief, there is virtually no possibility of causing oil-inspiration pneumonia, and indeed no adverse reactions have resulted from this squeeze-bottle method of olfactory testing.

The many potential applications for clinical olfactory threshold testing have been reviewed elsewhere, e.g. Henkin (1967), Schneider (1967), Alter and Seltzer (1974), Van Den Eeckhaut (1978) and Doty (1979). We find that in regular otorhinolaryngic practice the hyposmic and normal ranges of sensitivity require the most frequent testing (pyridine steps 6 through 13 and 14 through 21 respectively), though referrals from other departments, especially Endocrinology and Psychiatry, may involve the hyperosmic range as well (steps 22 through 29). For research purposes it may be necessary to employ each binary step, but, in clinical practice, test kits containing just the alternate (even-numbered) steps provide adequate precision. Some current examples of applications of this test method include the following: Testing patients before and after rhinoplasty, septal correction, etc., to demonstrate that olfactory function has been retained, or even improved. Evaluating insurance claims of hyposmia resulting from traumatic injury, occupational exposure, or medical malpractice. Clinical trials of suggested treatments for uncomplicated hyposmia, such as oral zinc sulfate or topical corticosteroids.

We believe that the ready availability of this practical and accurate test method will encourage more frequent use of quantitative olfactory testing in the course of clinical evaluation, diagnosis and treatment.

RÉSUMÉ

Un jeu de bouteilles en plastique polypropylène, contenant des dilutions en série de pyridine en huile minérale, est utilisé pour présenter au nez des bouffées d'air odorisé avec précision. Une measure quantitative du seuil olfactif du patient s'effectue ainsi en quelques minutes, le résultat pouvant être placé dans la classification de sensibilité normale, hyposmique ou hyperosmique.

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