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# Measurement of the blood flow of the nasal mucosa by the hydrogen clearance method

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SUMMARY

*The tissue blood flow of the nasal mucosa in normal subjects and patients with nasal allergy was studied by the hydrogen clearance method.*

*The flow in the inferior turbinate in normal subjects and patients with nasal allergy did not differ. The test results were highly reproducible and were almost the same in different anterior parts of the inferior turbinate.*

*The effects of nasal spray with vasoconstrictor and nasal provocation by an allergen-containing paper disc on the blood flow of the inferior turbinate were examined in normal subjects and patients with nasal allergy. The flow decreased remarkably after spray with vasoconstrictor. The flow also decreased remarkably in the mucosal membrane close to the area of contact of the allergen disc, whereas it increased at the area 10 mm away from the disc.*

*The hydrogen clearance method is useful for clinical studies of nasal circulation.*

## INTRODUCTION

Photoelectric plethysmography, polarography or the thermoconductivity method have conventionally been employed in studies of the circulation of the nasal mucosa. However, reliable values of the tissue blood flow per volume of tissue cannot be obtained by these methods from the theoretical point of view.

Therefore, we have studied the tissue blood flow of the nasal mucosa in normal subjects and patients with nasal allergy by the hydrogen clearance method. This method is based on Kety's theory (1951), which referred to Fick's principle. Aukland et al. (1964) first proposed a method for measuring the local blood flow in tissue, using polarographic recording of the clearance of hydrogen by means of platinum electrodes and actually applied this method to the myocardium, kidney and skeletal muscles. Subsequently, this method was applied to the brain by Fieschi et al. (1965). Since this method has not yet been applied to the nose, we investigated its usefulness in the study of the pathophysiology of nasal allergy.

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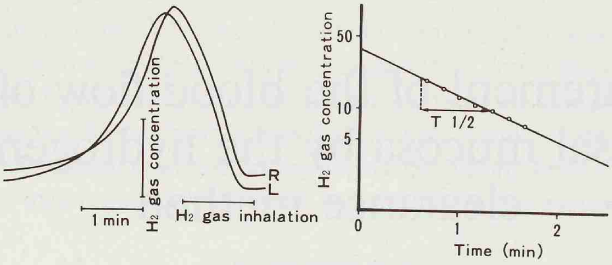


$F = 0.693 / T_{1/2}$ ml/min/g

F ; tissue blood flow

$T_{1/2}$ ; half decay time

Figure 1. The hydrogen concentration was measured through electrodes during inhalation of hydrogen. The hydrogen desaturation curve shows a single exponential decay as indicated on the left side of this figure. The half decay time is obtained from the slope of a tissue desaturation curve plotted on a semi-logarithmic scale against time as shown on the right side. The blood flow is calculated from the equation proposed by Aukland, $F = 0.693/T^1/_2$ ml/min/g, where $T_{1/2}$ is the half decay time of the hydrogen concentration.

## MATERIALS AND METHODS

The measurements were carried out in 24 normal adults and 38 patients with nasal allergy. The subjects were comprised of 32 men and 30 women ranging in age from 13 to 41 years old. The hydrogen concentration in the inferior turbinate of the subjects was measured through platinum electrodes 300μ in diameter that were inserted 1 mm into the mucosa of the inferior turbinate during inhalation of hydrogen. Clearance curves were recorded with a polygraph by M.T.PHG-300. Blood flow values of the inferior turbinate were calculated by a compartmental manual analysis of the clearance curves on semilogarithmic paper (Figure 1). The provocation test used has been described elsewhere (Okuda, 1974). Briefly, an allergen-containing small round paper disc is placed on the surface of the anterior part of the inferior turbinate. Responses induced were graded by the three allergic manifestations, i.e., (1) sneezing or itchiness, (2) the increase of nasal secretion and (3) swelling of the mucous membrane; the appearance of two or more of these symptoms was regarded as a positive response and classified as 1+, the appearance of three symptoms with sneezing less than five times was classified as 2+ and with sneezing more than six times as 3+.

## RESULTS

The means and standard deviations of the tissue blood flow of the inferior turbinate in normal subjects and patients with nasal allergy were $1.13 \pm 0.31$ ($n = 107$) and $1.18 \pm 0.33$ ml/min/g ($n = 103$), respectively. Statistically, no significant difference was found between them. Additionally, no statistically significant differences were noted by age or sex.

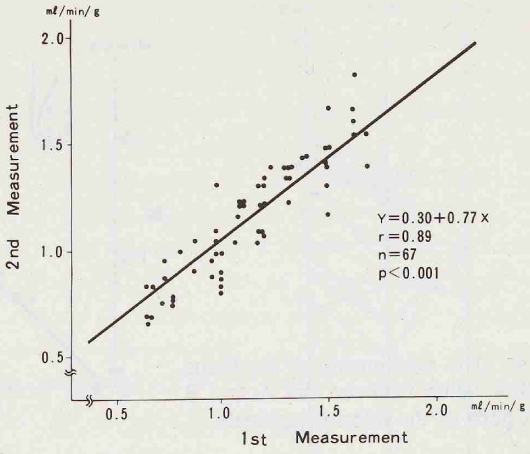


Figure 2.
Reproducibility in the hydrogen clearance method (in normal subjects).

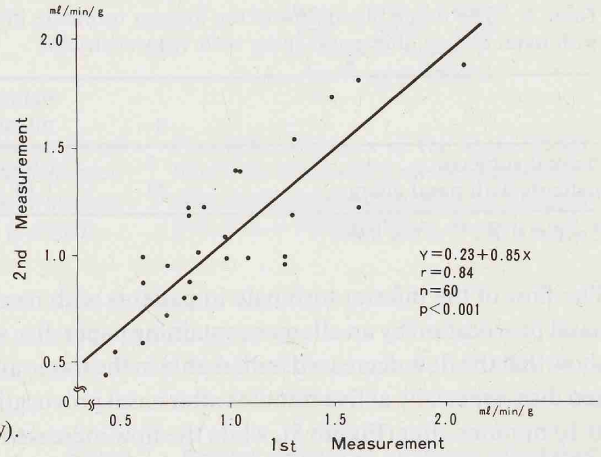


Figure 3.
Reproducibility in the hydrogen clearance method (in patients with nasal allergy).

The measurements were repeated at least twice in each subject at an interval of about 10 minutes. As shown in Figures 2 and 3, the values of the tissue blood flow at the first and second measurements were found to be very similar. This indicates the high reproducibility of this measurement method.

Two electrodes were inserted into the anterior part of the same inferior turbinate at a distance of 10 mm, and the blood flow was measured simultaneously. As shown in Figure 4, the tissue blood flow was almost the same if the position of the electrodes was limited to within the anterior part of the inferior turbinate.

The effect of nasal spray with vasoconstrictor, which is generally used in our clinic, on the flow in the inferior turbinate in normal subjects and patients with nasal allergy was measured. As shown in Table 1, the tissue blood flow decreased remarkably and rapidly after nasal spray with vasoconstrictor.

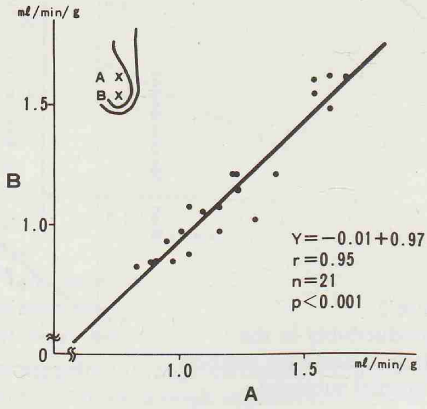


Figure 4. The relationship of the tissue blood flow value between the A and B anterior parts of the inferior turbinate.

Table 1. The tissue blood flow of the inferior turbinate in normal subjects and patients with nasal allergy after nasal spray with vasoconstrictor.

| | n | before ml/min/g | 5 min. ml/min/g |
|---|---|---|---|
| normal subjects | 7 | 0.93 ± 0.08 | 0.65 ± 0.18* |
| patients with nasal allergy | 33 | 1.19 ± 0.40 | 0.91 ± 0.29** |

* = $p < 0.01$, ** = $p < 0.001$

The flow of the inferior turbinate in patients with nasal allergy before and after nasal provocation by an allergencontaining paper disc was measured. The results show that the flow decreased remarkable in the tissue at the area close to the allergen disc, especially at five minutes after nasal provocation, and tended to recover at 10 minutes after (Figure 5), while the flow increased in the tissue 10 mm from the disc, especially at five minutes after nasal provocation, and tended to recover at 10 minutes (Figure 6). Percent changes of the blood flow before and after nasal provocation were compared with the degree of the nasal provocation test. The flow in the tissue at the area close to the allergen disc decreased with significant correlation to the strength of the nasal response, whereas that in the area away form the disc increased remarkably in proportion to the nasal response (Figure 7).

## DISCUSSION

The present study clearly demonstrated that the hydrogen clearance method is a useful tool for evaluating the blood flow of the nasal mucosa because of continuous measurement of the nasal blood flow without blood sampling, the high reproducibility and minimum variation of values obtained from different sites of the anterior part of the inferior turbinate. However, there are still some problems to

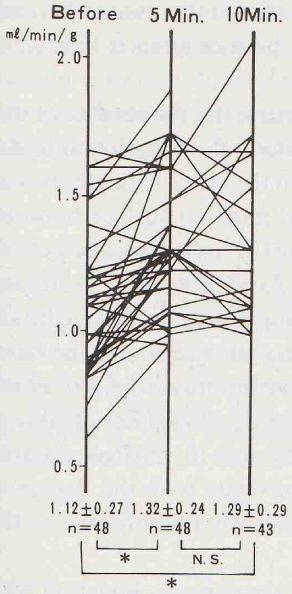


Figure 5. Changes in the tissue blood flow at the area of contact of the allergen disc after nasal provocation with an allergen disc. N.S. = not significant, * = $p < 0.001$.

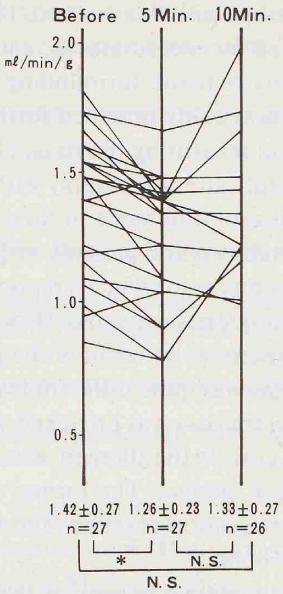


Figure 6. Changes in the tissue blood flow at the area away from the allergen disc after nasal provocation with an allergen disc. N.S. = not significant, * = $p < 0.001$.

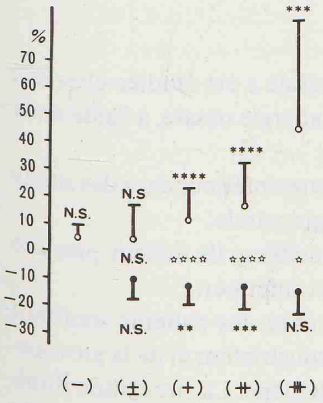


Figure 7. Percent changes of the tissue blood flow before and after nasal provocation were compared with the degree of the nasal provocation test. The filled circles and bars indicate the means and standard deviations of the local flow close to the disc, and the open circles and bars show the means and standard deviations of the flow in the tissue 10 mm away from the disc. * shows statistical difference in percent changes of the flow between before and after nasal provocation. ✧ shows statistical difference of the flow between near the disc and away from the disc. The flow at the area close to the allergen disc decreased with a significant correlation to the degree of nasal response, while that at the area far from allergen disc increased as the nasal response increased.
N.S. = not significant, ✧ = $p < 0.05$, ** = $p < 0.02$, *** = $p < 0.01$, ****, ✧✧✧✧ = $p < 0.001$.

be overcome with this method. The electrode always injures the tissue when it is punctured for measurement, and the blood flow to be measured is limited to small area of tissue surrounding the electrode.

The present study provided further evidence supporting the reliabiality of this method in measuring the nasal blood flow, i.e., the blood flow was found to decline rapidly after nasal spray with vasoconstrictor. On the other hand, there was no significant difference in flow volume of the nasal mucosal surface between normal subjects and patients with nasal allergy during the asymptomatic period. This is contrary to Okuda's report (1974) stating that nasal blood flow decreased in the allergic nasal mucosa. However, we can overcome this contradiction by another experimental result of the present study. During allergic attack, the nasal blood flow was quite different from that during the asymptomatic period. When the nasal mucosa was provoked with allergen, the flow decreased remarkably at the area close to the allergen, whereas it increased at the area 10 mm from the area of allergen contact. The former change tended to correlate with the degree of nasal provocation reaction, and the latter was significantly proportional to the nasal response.

This phenomenon resembles the skin reaction to intracutaneous injection with allergen extract. Wheal (stasis of blood flow and edema) occurs at the site of allergen injection, erythema (dilatation of vessels and increased blood flow) is produced around the injection site, and the sizes of the wheal as well as the erythema express the degree of skin reaction. The decrease of the nasal blood flow produced by nasal provocation may correspond with the condition of the blood flow in the wheal in the skin reaction, and the increase may be connected with that in the erythema. Granting this to be true, the present method may possibly provide us with valuable information for better understanding of the patho-physiology of the nasal mucosa.

RÉSUMÉ

La circulation sanguine tissulaire de la muqueuse nasale a été étudiée chez des sujets normaux et chez des patients souffrant d'une allergie nasale, à l'aide de la méthode de déconcentration d'hydrogène.

Il n'y avait pas de différence de circulation dans le cornet inférieur chez des sujets normaux et chez des patients souffrant d'une allergie nasale.

Les résultats des essais étaient hautement reproducibles; ils étaient presque égaux dans différentes parties antérieures du cornet inférieur.

Nous avons examiné, chez des sujets normaux et chez des patients souffrant d'une allergie nasale, les effets d'un spray avec vasoconstricteur et de la provocation nasale par un disque en papier contenant un allergène. La circulation diminuait remarquablement après l'application du spray avec vasoconstricteur; elle

diminuait aussi remarquablement dans la membrane muqueuse se trouvant près de l'aire de contact du disque allergène, tandis qu'elle augmentait dans l'aire se trouvant à 10 mm du disque.

La méthode de déconcentration d'hydrogène est utile pour des études cliniques de la circulation de la muqueuse nasale.

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