

# Clinical and Experimental Study on Thermoregulatory System and its Relation with Vasomotor Rhinitis

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## ABSTRACT

### Introduction

Much of the perennial cold are of vasomotor origin still a less appreciated phenomenon even among the medical personnel, much of which is dubbed in a cursorily in the clinical analogue of a west paper wrap as 'allergic rhinitis'. This study was attempted to find out the role of thermoregulatory system with causation of vasomotor rhinitis and assessing role of hypothalamus in causation of vasomotor rhinitis.

### Materials and Methods

In this study conducted during the period of July 1987 to August 1988, 20 normal adult individuals were taken as control and thermoregulatory study was done on them. The results were compared with cases of vasomotor rhinitis/non-allergic rhinopathy cases. In experimental study thermoregulatory study was done on albino rats before and after stereotaxis of anterior and posterior hypothalamic nuclei and the result were compared before stereotaxis and post stereotaxis.

### Results

Among human study in clinical subjects, patient suffering from vasomotor rhinitis showed a definite shift towards thermoregulatory imbalance both for generalized body caloric fluctuation and particularly on the nasal mucosa. Post-vidian neurectomy results for thermoregulation test was highly significant. In animal study post-hypothalamic stereotaxis temperature measurement showed minimal depression. Dorsal anterior hypothalamic lesion ablation showed significant derangement in the thermoregulatory tolerance profile of the rats' belly temperature. Posterior hypothalamic lesion showed that there may be some amount of derangements in the thermoregulatory tolerance, which however is not statistically conclusive. Thermoregulatory control is done at hypothalamus, particularly at anterior hypothalamic nuclei level and posterior hypothalamic nuclei in the brain. Thermoregulatory study proves a close correlation between non allergic rhinitis with imbalance in central thermal regulation by hypothalamus.

### Conclusion

Thermoregulatory study in control and clinical subjects proves a close correlation between vasomotor rhinitis and sympathetic, parasympathetic system.

### Keywords

Rhinitis, Vasomotor; Body Temperature Regulation; Autonomic Nervous System; Hypothalamus; Denervation

The term nonallergic vasomotor rhinitis (also called idiopathic rhinitis) means rhinitis symptoms that occur in relation to nonallergic, noninfectious triggers like: changes in temperature, humidity, and barometric pressure; exposure to strong odours, tobacco smoke, and exhaust fumes; and even the ingestion of certain foods. Up to 33 % of patients with rhinitis are estimated to be of nonallergic rhinitis, and close to 65% of patients with allergic rhinitis also have symptoms that occur or worsen in the presence of nonspecific, nonallergic stimuli.<sup>1</sup>

Usually the primary symptoms observed are nasal

obstruction and rhinorrhoea, with the term "vasomotor" suggesting involvement of neural, glandular, and vascular pathways.

Vasomotor rhinitis is the most common form of nonallergic rhinitis, comprising approximately 71%

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of all nonallergic rhinitis conditions.<sup>2</sup> Its etiology and pathogenesis are imperfectly understood. Its diagnosis especially differentiation from other groups of rhinitis is difficult. The natural history is also variable and sometimes it remains undiagnosed in presence of other disabling diseases. Its treatment is also controversial and has changed from time to time. Due to rich autonomic supply of the nose, minimal changes of temperature, any neuroendocrinal change and emotional change can affect the nasal mucosa to a greater or lesser degree. Although the unified airway hypothesis indicates shared pathophysiological processes across both the upper and lower airways,<sup>3-5</sup> the role of the autonomic nervous system (ANS) in nose and sinus symptoms is poorly understood. Historically, the capacity of the nasal vasculature to shrink and engorge in animals was known in the 1850s and was histologically characterized as early as the 1950s.<sup>6</sup>

The important vasomodulatory effects of autonomic nerves in the nose were highlighted by Millonig et al<sup>7</sup> in 1950 and further supported by evidence from cases of autonomic denervation in patients with nose symptoms. Konno and Togawa described, in 1979, the successful use of a vidian nerve section to improve symptoms of patients' allergic rhinitis.<sup>8</sup> However, the transient results and variable benefits for different symptoms indicate a more complex relationship between the nose and the ANS. Alexander et al in their research studied the role of ANS dysfunction in sinonasal disease. The ANS is influenced by multiple factors, including personality and psychological distress, that causes the sinonasal symptoms. Further research will help to clarify the etiology of ANS dysfunction and its contribution to common systemic conditions.<sup>9</sup> As hypothalamus is controlling the sympathetic and parasympathetic system of the body it is postulated that any hypothalamic imbalance specially changes in the molecular level and neurotransmitter level can cause a minimal sympathetic parasympathetic imbalance which can affect the thermoregulatory system of the body. This derangement of the thermoregulatory system can also occur via any endocrinal changes which also work through hypothalamus. In the present study, we tried to find out the role of thermoregulatory system and hypothalamus in the causation of vasomotor rhinitis.

## Materials and Methods

### CLINICAL MATERIAL:

The material of this clinical study consisted of 30 cases of vasomotor rhinitis and 20 controls seen and treated at Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry during the period of July 1987 to August 1988.

### CASE:

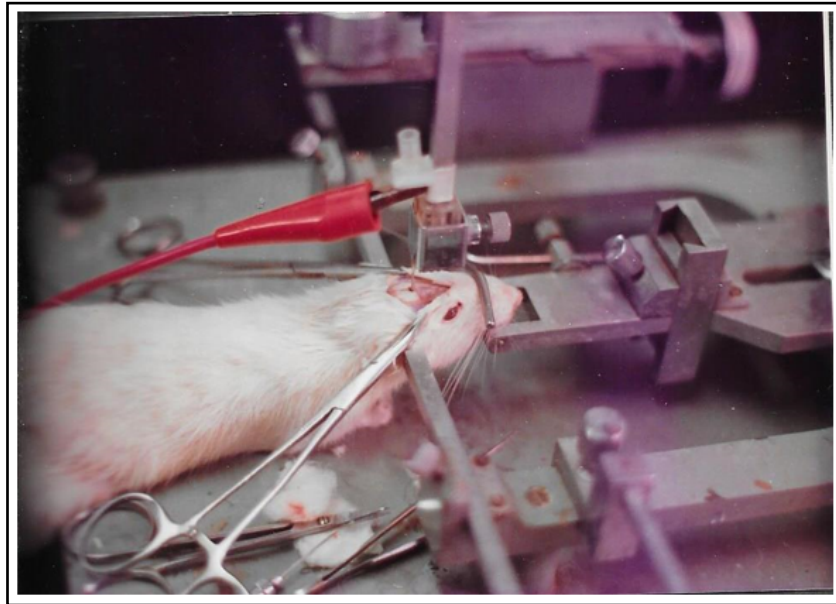
A case of vasomotor rhinitis was diagnosed based on the following criteria:

- 1) More than two attacks of rhinorrhoeic bouts/month.
- 2) History of intolerance to temperature variation.
- 3) Alternate or both nostrils having persistent nasal blockage or nasal blockage without any general signs of nasal inflammation like malaise and fever.
- 4) Pale or congested edematous mucosa of nasal turbinates without any mucopus.
- 5) Radiology suggestive of mucosal hypertrophy with or without polypoidal changes, but not exhibiting any fluid level.
- 6) Nasal smear and peripheral blood not showing eosinophilic preponderance i.e. less than 6 cells/field which is normal in this area.

Any patient fulfilling a minimum of four criteria from the list above, including sixth which is the most confirmatory sign, was taken into the pool of our study.

### CONTROL:

Normal adult siblings of the patients were studied (Total 20). After all this preliminary investigation, experimental study on control & clinical subjects was conducted to examine the thermal influence on causation of cold. All the experiments were conducted in a thermoneutral laboratory (temperature  $26 \pm 1^\circ \text{C}$ ) using an indigenously devised thermocouple incorporated to 7P1 preamplifier of Grass Model 7 Polygraph with DC 15 Hz as low frequency and high frequency. The speed of the recording was usually 0.25 mm/sec. Normal palm and nasal mucosal temperature were recorded on clinical



**Fig. 1. Hypothalamic stereotaxis (anterior and posterior)**

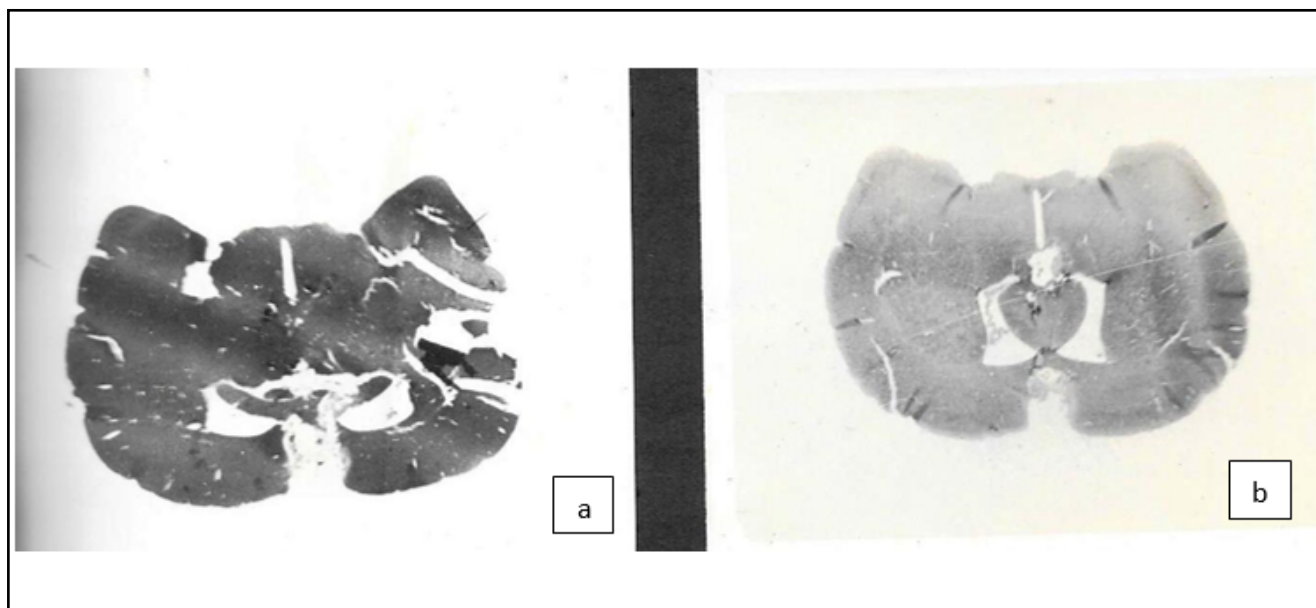
experimental subjects. After that all the experimental subjects were challenged with sudden exposure to cold. Cold challenge was presented to hand and nose.

The palm of the hand was cooled by dipping into ice cold water at  $12^{\circ}\text{C}$  for 3 minutes. Water from the hand was soaked by a filter paper to prevent heat gain by manual rubbing with towel. After that temperature of the palm was measured again for ten minutes and the time period over which the temperature of the palm regains its normal value was recorded. Similarly, the nose was irrigated with ice cold water at  $12^{\circ}\text{C}$ . Residual water in the nasal cavity was soaked by keeping a piece of the filter paper in the dependent portion of the nose. Nasal temperature was recorded again and the time period over which it comes to its normal value was also recorded. During the post cooling temperature measurement, patient is asked to breathe through mouth, so that no caloric exchange took place between nasal air current and respiratory mucosa. Twenty controls were studied to evaluate the normal values.

Another series of 10 patients were taken up from the post vidian neurectomy group to note whether temperature changes can occur in the nasal mucosa after vidian nerve section.

#### EXPERIMENTAL STUDY:

Experimental study on western Albino rats was done to know the influence of autonomic nervous system on mammalian nasal mucosa. A total of twenty rats were used for the experimental purpose to assess the autonomic denervation at the level of hypothalamus and its relationship with cold exposure. In ten experimental rats, dorsal anterior hypothalamus stereotaxis was done with the help of neurophysiologist. (Fig. 1) Coordinates for the desired area of lesion were determined according to stereotaxis atlas for the rats.<sup>10</sup> Stereotaxis apparatus (INCO) was used. Bilateral electrolytic lesions were made by using a current of two to three amperes from INCO lesion maker for fifteen seconds. Before the lesion all the rats' normal belly temperature and post cooling temperature (after cooling with  $12^{\circ}\text{C}$  water for 3 minutes) of the belly were recorded. Post lesion rats were again then subjected to thermoregulatory study after 3 weeks to examine any post stereotaxis temperature variation with cold challenge test and the results were analyzed. Similarly, posterior hypothalamic lesion was done in 10 albino rats. (Fig. 2)



**Fig.2. Rat Brain section showing electrolytic lesion in a) Posterior hypothalamus, b) Anterior hypothalamus.**

## Results

Thermoregulatory profile was done for control group and clinical patients. Experimental cold challenge test was done in both groups and the temperature changes are measured by a thermocouple attached with Grass Model 7 Polygraph.

Control group shows return to normal temperature after initial cooling of hand and nasal mucosa for specified time as per methodology already described. Mean period of return to normal temperature in hand was 335.5 sec. varying from 200 to 600 seconds. In nose the mean period to return to normal temperature 101.58 sec. varying from 80 -120 seconds (Table I)

Vasomotor rhinitis patients show a poor vasomotor response as evidenced by a delayed return to normal temperature (Mean value in hand 746 sec., mean value in nose 250.5 sec). All the data are subjected to statistical analysis by unpaired 't' test and compared to normal and 'p' value calculated. In both hands and nose it is less than 0.001 which is highly significant (Table II).

Post-vidian neurectomy patients (Table III) were examined similarly. Their hands' temperature record was still abnormal but time period over which the nose was coming back to normal after cold challenge test,

shows a major shift towards normalcy (Mean value 263 sec. to 103 sec.). Statistical analysis was done by paired 't' test and 'p' value calculated ( $P < 0.001$ ) which was highly significant.

## ANIMAL EXPERIMENT:

A total of 20 rats were used for this experiment. In 10 rats, dorsal anterior hypothalamic stereotaxis was done. Before the lesion, all the rats' belly temperatures were measured. Average belly temperature for the control rats was 34-37°C. Cold challenge test was done on the rats' belly and temperature was recorded. Similarly, temperature was recorded after the lesion using thermocouple and Grass Model 7 Polygraph.

Temperature was recorded in rats with posterior hypothalamic lesion also in similar manner. After anterior hypothalamic stereotaxis there was elevation of the belly temperature ranging from 34.6°C to 39°C, average 37.61°C. In posterior hypothalamic lesion, it was observed that there was a minimal lowering of the body temperature ranging from 32-37°C (Mean value 34.25°C). All the data were statistically analyzed (paired t test) and p value was calculated. It was seen that p value was significant for anterior hypothalamic

Table I: Control group of patients

SL. NO.	NORMAL TEMPERATURE		AFTER COLD CHALLENGE TEST (AVERAGE TIME TAKEN TO COME BACK TO NORMAL)	
	HAND TEMP(°C)	NOSE TEMP(°C)	HAND	NOSE
1	33	34	600 sec	80 sec
2	34	33	440 sec	90 sec
3	35	34	200 sec	100 sec
4	33	34	330 sec	90 sec
5	36	36	400 sec	100 sec
6	35	35	360 sec	100 sec
7	33	34	200 sec	100 sec
8	31	35	380 sec	120 sec
9	33	33	280 sec	90 sec
10	32	35	200 sec	110 sec
11	33	35	260 sec	60 sec
12	30	34	280 sec	115 sec
13	34	35	400 sec	120 sec
14	32	37	280 sec	110 sec
15	32	38	300 sec	115 sec
16	33	31.5	360 sec	90 sec
17	32	32.5	400 sec	80 sec
18	34	33	400 sec	140 sec
19	32	32.5	360 sec	120 sec
20	33	-	280 sec	-

lesion (p value <0.001). (Table IV)

### Discussion

The hypothalamus is a very small, but extremely important part of the diencephalon that is involved in the mediation of endocrine, autonomic and behavioral functions. Recent studies divide the hypothalamus

rostrocaudally into four regions: preoptic, supraoptic, tuberal, and mammillary regions. Each region consists of several nuclei, whose functions were defined mainly using lesions, stimulations, and genetic approaches. The anterior hypothalamic nucleus is a nucleus of the hypothalamus. Its function is thermoregulation (cooling) of the body. Damage or destruction of this nucleus causes hyperthermia. The anterior hypothalamic

Table II: Patients selected for surgery (Vasomotor Rhinitis)

SL NO.	NASAL TEMP(°C)	HAND TEMP(°C)	TIME TAKEN FOR HAND TEMPERATURE TO COME BACK TO NORMAL AFTER COLD CHALLENGE(SEC)	TIME TAKEN FOR THE NASAL TEMPERATURE TO COME BACK TO NORMAL (SEC)
1	31	31	1200	240
2	32	31	680	240
3	35	35	600	250
4	34	35	880	280
5	35	33	680	280
6	35	32	800	260
7	33	32	700	280
8	34	35	600	220
9	35	35	520	220
10	37	33	500	240
11	35	37	800	200
12	36	32	960	280
13	36	32	760	360
14	34	33	680	250
15	32	34	700	220
16	34	33	800	270
17	34	33	900	260
18	36	34	760	200
19	35	32	800	220
20	34	31	600	240

region is sometimes grouped with the preoptic area.<sup>11</sup> The posterior nucleus of the hypothalamus is one of the many nuclei that make up the hypothalamic region of the brain. Its functions include elevation of blood pressure, pupillary dilation, and shivering or body heat conservation (thermoregulation).<sup>12</sup>

The hypothalamus has the most complex circuitry of any brain region. Like other brain areas there are neural

interconnections. But unlike other brain areas, there are also extensive non-neural communication pathways between the hypothalamus and other brain regions and the periphery.

The circuits are named as limbic circuits, sensory and autonomic circuits and neuro-humoral connections. The role of the hypothalamus in regulation of homeostasis is result of proper interconnection between these circuits.



**Table III: Estimation of nasal temperature before and after vidian neurectomy.**

SL. NO.	BEFORE SURGERY		AFTER SURGERY	
	NASAL TEMP (°C)	TIME TAKEN FOR NASAL TEMP TO COME BACK TO NORMAL(SEC)	NASAL TEMP (°C)	TIME TAKEN TO COME BACK TO NORMAL TEMP(SEC)
1	34	280	35	120
2	35	280	36	100
3	35	260	36.5	80
4	33	280	38	90
5	34	220	37	110
6	35	220	35	100
7	37	240	36.5	120
8	35	200	37	110
9	36	280	36.5	90
10	36	360	36	110

*The above data was subjected to "Paired" 't' test.*

*Before Surgery: Average value = 262 sec. S.D = 45.65 sec. S.E = 4.22 't' value = 10.34*

*After Surgery: Average value = 103 sec. S.D = 13.37 sec. S.E = 4.23*

*Degree of freedom 9*

*After surgery on comparison 'P' value is <0.001 (Significant)*

Insult on one circuit results in disturbances in other. We by our experimental and clinical study tried to establish relationship of the thermoregulatory circuits with vasomotor rhinitis which is an autonomic dysfunctional problem.

Adaptive heat production (thermogenesis) in a cold environment, such as shivering, is triggered by cold sensation delivered from thermoreceptors in the skin to the thermoregulatory brain centre, preoptic area (POA) of the hypothalamus. The thermosensory information from the skin is transmitted to the lateral parabrachial nucleus (LPB) of the brainstem through the spinal cord and this information is further transmitted from the LPB to the POA. Cold and warm sensory pathways are mediated by separate populations of neurons in the

LPB. Rats whose spinal-LPB-POA neural pathways are interrupted cannot promptly produce heat in a cold environment, dissipate body heat in a hot environment, or choose comfort thermal environment, indicating that these thermosensory neural pathways play a critical role in autonomic and behavioral defense of body temperature from ambient cold and heat.<sup>13</sup>

The temperature change and its relation with nasal mucosa was studied by Drettner.<sup>14</sup> The nasal temperature showed a tendency to rise with rise in outdoor temperature. Cooling of the back was associated with decrease in nasal temperature and this cooling is greater in women than men. Also cooling of feet was accompanied by transient reduction of nasal temperature and this decrease is greater than cooling of back. The

Table IV: Animal Studies

SL. NO.	CONTROL	LESION I (POSTERIOR HYPOTHALAMIC LESION)	LESION II (ANTERIOR HYPOTHALAMIC LESION)
	TEMP MEASURED BY THERMOCOUPLE-FILLED WITH GRASS MODEL '7' POLYGRAPH (C)	TEMP MEASURED AFTER POSTHYPOTHALAMIC ELECTROLYTIC LESION (C)	TEMP MEASURED AFTER DORSAL HYPOTHALAMIC ELECTROLYTE LESION(C)
1	34.8	32	37
2	35	33	37
3	36	35	39
4	37	35	38
5	35	34	38
6	34	33	34.6
7	36	35	38
8	34.8	35	38
9	34	34	38.5
10	34	37	39
STASTICAL ANALYSIS (Paired 't' test)	Average value = 35.06 C	AV = 34.25 C	AV = 37.61 C
	Standard Deviation = 1.002	SD = 1.39	SD = 1.3
	Standard Error = 0.317	SE = 0.443	SE = 0.41

nasal passage exhibited gradually progressive narrowing especially marked after discontinuation of cooling. Also cooling of the inspiratory air caused pronounced fall of nasal temperature and nasal passage became narrower during inspiration of cold air. General skin cooling also caused the narrowing of nasal passage. They also did the same cooling experiment on persons with allergic or non-allergic rhinopathy at the period when subjects were in normal phase. There was marked swelling at the end of the cold which was in general similar to those in the normal persons. There was relatively pronounced tendency of blanching of nasal mucosa during the exposure to the cold, followed by a bluish discoloration.

In present study a poor thermoregulatory balance was noticed in all cases of vasomotor rhinitis in comparison

to control group, as evident by history of cold intolerance and cold challenge test in hand and nose ( $P < 0.001$ ) both in hand and nose by unpaired 't' test. Again, in post vidian neurectomy cases, hand temperature remains abnormal while the nose temperature is coming back to normal level ( $P < 0.001$  by paired 't' test – highly significant) due to parasympathetic ablation. This is due to very close relation of thermoregulatory centres in hypothalamus and its association with sympathetic-parasympathetic centre.<sup>15</sup> Any thermal stimulus can stimulate the thermoregulatory centre of the body on exposure to thermal change. This, in turn, causes an imbalance in sympathetic-parasympathetic system which act upon the very sensitive tissue of the nasal mucosa resulting in congestion and rhinorrhoea.



Dorsal anterior hypothalamic lesion: Temperature study after lesion of this region was suggestive of the hyperthermia indicating that parasympathetic and thermoregulatory centres are in very close proximity with each other and a dorsal anterior hypothalamic lesion can cause temperature imbalance in experimental albino rats ( $P < 0.001$ ). In anterior hypothalamic lesions the rectal temperature even reaches  $43^{\circ}\text{C}$  and anterior hypothalamus acts on the heat-dissipating centre of the body.<sup>15</sup>

Posterior hypothalamic lesion: In posterior hypothalamic lesion, thermoregulatory study showed there was minimal depression of the temperature in the post stereotaxis rat in comparison to the normal. (Average time 34.25 sec. 't' value 1.488, not significant).

Eccles and Lee found maximal vasoconstrictor response were elicited in the hypothalamus anterior to mammillary body and in the central grey matter of mesencephalon.<sup>16</sup> Secondly, there is central autonomic control which extended to area 6 and 8.

## Conclusion

Thermoregulatory control is done at hypothalamus, particularly at anterior and posterior hypothalamic nuclei in the brain. Thermoregulatory study in control and clinical subjects proves a close correlation between vasomotor rhinitis and sympathetic, parasympathetic system via hypothalamus in the body.

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## Statement of informed consent

Informed consent taken from all the clinical & control subjects on a preformed proforma.

## Statement of human and animal rights

The first author states with supporting documents that he had necessary permission from the institution to perform the procedures.

## Editor Comments

Though the study was conducted in 1986-87, the findings of the study are still relevant and studies on this subject are very few since then.

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