

Epidemiologic study of excessive oral melanin pigmentation with special reference to the influence of tobacco habits

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Abstract - The prevalence of oral melanin pigmentation was studied in a population of 30 118 adult individuals in Sweden. Among these, 9.9% showed melanin pigmentation in the oral mucosa. The anterior labial gingiva in the mandible was the most frequently pigmented location. The presence of melanin pigmentation was positively correlated to tobacco smoking. Among tobacco smokers 21.5% were pigmented as compared to 3.0% among individuals not using tobacco. The smoking-related oral pigmentation, smokers' melanosis, could thus be calculated at a prevalence of 18.5% among smokers and the total frequency of smokers' melanosis was calculated at 6.8%. The prevalence of pigmentation was found to increase prominently during the first year of smoking but also to decrease to the level found among non-tobacco users about 3 years after cessation of smoking. Snuff dipping did not significantly elevate the prevalence of oral melanin pigmentation.

Key words: Caucasoid race; epidemiologic methods; gingiva; melanocytes; melanoplakia; mucous membrane; sex; snuff; smoking; time factor.

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Oral melanin pigmentation is sometimes seen in connection with rare pathological conditions such as Addison's disease or Peutz Jeghers' syndrome (1, 2). More frequently oral melanin pigmentation has been reported among healthy individuals, e.g. in dark skinned ethnic populations to a prevalence of almost 100% (3), and in Asians between 30 and 98% (4, 5). Compared to findings among these ethnic groups the prevalence of oral melanin pigmentation among light skinned Caucasians is reported to be relatively low, 5-10% (6, 7). Accordingly the prevalence of oral melanin pigmentation in

healthy individuals has been considered to be correlated to the degree of skin pigmentation (8), and thus to be linked primarily to genetic factors. However, a connection between tobacco smoking and oral melanin pigmentation has been suggested (9-11). This hypothesis has been confirmed in a study on gingival melanin pigmentation in a selected group of patients in northern Sweden (12). A strong correlation was found between cigarette smoking and gingival melanin pigmentation, also among individuals with blond hair and blue eyes. The pigmentation was labeled smokers' melanosis. It was predicted

that other locations than the gingiva might be more frequently pigmented among smokers than among non-smokers.

The aim of the present investigation was to assess the correlation between excessive oral melanin pigmentation and different tobacco habits. The aim was also to study the distribution of pigmentation in the oral cavity and to compile data on the pigmentation with reference to demographic data such as age and sex.

Material and methods

All information for this study was collected in connection with the undertaking of a basic project aimed at assessing prevalences of oral mucosal lesions in an adult Swedish population. The study was carried out 1973-74 (7). In the central part of Sweden a general population consisting of urban, suburban and rural inhabitants aged 15 years or older was examined. The total number of people summoned for examination was 30 118. Of these, 18 659 attended and were examined. The non-participants became the subject of a special investigation for which every fifth individual, 2292 persons, was randomly sampled. After a second summons, 933 persons attended for examination and through personal contacts an additional 741 individuals could be examined in private homes, places of work, hospitals, old age homes and other institutions. In total, 20 333 people (10 036 males and 10 297 females) could thus be examined. This corresponded to a frequency of participation of 89.7% provided that the examined non-participants were weighted by a factor of five. The mean age of the population was 43.0 years (males 42.6 years and females 43.4 years).

Oral pigmentation was labeled 'excessive melanin pigmentation NOS' (*not otherwise specified*) in accordance with the WHO publication ICD-DA (1973). Clinical criteria set forth for that diagnosis (including melanoplakia) were

Macules or diffusely outlined areas of brown to brownish-blue colour. The lesion cannot be classified as due to exogenous pigmentation.

Information on tobacco habits was collected on pretyped forms before the patients were clinically examined. The examiner was not aware of the information given.

The reliability of the clinical registration was tested

by means of reexamining 256 consecutive individuals recalled for biopsing various mucosal lesions. The probability of registering a pigmentation at both examinations if it was registered in any of them was 0.78. The reliability of information given on tobacco habits was tested through questioning 278 consecutive individuals 1-2 weeks after the first questioning. Diverging information was given by 3.4% individuals who, at the time of questioning, referred to unchanged habits and by 76.5% by individuals who referred to having changed their tobacco habits (13).

Among the 20 333 individuals examined, 8048 (39.6%) had some daily tobacco habit, while 10 757 (52.9%) did not have any tobacco habit at all. Another 1489 (7.3%) individuals reported that they used tobacco occasionally. For 39 (0.2%) information was insufficient.

Calculations of prevalences were carried out through a weighting procedure where due consideration was given to number of lesions found and frequency of participation in different demographic groups. The prevalence in the *i*-th demographic group was calculated as

$$p_i = \frac{1}{N_i} \left(x_{i1} + \frac{M_{i2}}{m_{i2}} x_{i2} \right), \text{ where}$$

p_i = prevalence of pigmentation

N_i = total number of individuals

x_{i1} = number of individuals with pigmentation found among people attending after the first summons,

M_{i2} = number of primary non-participants,

m_{i2} = total number of primary non-participants subsequently examined, and

x_{i2} = number of individuals with pigmentation found at examination of primary non-participants.

Occurrence not calculated by this procedure was simply calculated by dividing the number of pigmented individuals with the total number of those examined. Below, occurrences calculated in this way will be referred to as *frequencies* as opposed to *weighted prevalences*. Prevalence differences between groups were tested by means of estimating the quantity

$$z = \frac{p_a - p_b}{\sqrt{SE(p_a)^2 + SE(p_b)^2}}, \text{ where}$$

p = prevalence, a = group a , and b = group b .

When the total prevalence was lower than 2% the findings were not considered approximately $n(0.1)$ -distributed. Differences were then tested by means of a

chi-square test, which was also used when calculating differences of frequencies between groups. The following levels of significance were used

n.s. (not significant) $0.05 < P$
 * $0.01 < P < 0.05$
 ** $0.001 < P < 0.01$
 *** $P < 0.001$

Moderate cigarette smokers were defined as individuals consuming not more than 15 cigarettes a day. Individuals consuming more were classified as heavy cigarette smokers.

Results

PREVALENCES

The prevalence of oral melanin pigmentation in the investigated population was 9.9%. The pigmentation was most prevalent in the age group 25–34 years, 15.9%. The prevalence increased up to this age group and decreased thereafter, most distinctly above the age group 45–54 years (Table 1). No statistically significant difference was found between the sexes, the prevalence being 10.5% for males and 9.4% for females.

LOCATION OF PIGMENTATION

The most frequently pigmented locations are given in Table 2. The attached gingiva in the anterior part of the mouth was by far the most affected location, and then especially in the mandible. In a downward order of frequency pigmentation was found in the buccal mucosa, the buccal gingiva in the molar and premolar regions, the vermillion border of the lips and the lingual gingiva in the mandible. Pigmentation was very rare in the hard and soft palate, on the tongue and in the vestibular areas. In no case was pigmentation found at the apex of the tongue or in the vestibular mucosa in the anterior areas of the mouth. As regards location of pigmentation there were no sex differences. In Fig. 1 relative frequencies of pigmentation are indicated in different regions of the mouth. The figures express, for each location, the percentage of all individuals pigmented in that special location.

TOBACCO HABITS

Among daily tobacco users only those with exclusively one tobacco habit were included in

Table 2

Number of individuals with and prevalence (percent) of oral melanin pigmentation among 20333 individuals. Distribution according to sex and oral location

Location	Males		Females		Total	
	n	%	n	%	n	%
Anterior labial alveolar process, mandible	792	7.9	687	6.7	1479	7.3
Anterior labial alveolar process, maxilla	456	4.5	431	4.2	887	4.4
Buccal mucosa	195	1.9	158	1.5	353	1.7
Vermillion border	64	0.6	52	0.5	116	0.6
All regions	1040	10.4	919	8.9	1959	9.6

the calculations. Moderate cigarette smoking was most prevalent among females while all other habits were more frequent among males. The frequency of tobacco smokers within different age groups are shown in Table 1. For males the frequency was just over 30% in all age groups up to 65–74 years. Among females tobacco smoking was much more frequent in younger than in older age groups.

TOBACCO HABITS AND PIGMENTATION

Among non-tobacco users (also including previous tobacco users) 3.0% showed pigmentation (Table 3). Cigarette and pipe smokers showed significantly higher prevalences, 21.9% and 16.8%, respectively ($P < 0.001$). In contrast, snuff dippers did not show a higher prevalence of pigmentation, 4.7%, as compared to non-

Table 1

Number of individuals with and prevalence (percent) of oral melanin pigmentation, and frequency (percent) of tobacco smokers among 20 333 individuals. Distribution according to age and sex

Age, years	Pigmented individuals						Tobacco smokers	
	Males		Females		Total		Males	Females
	n	%	n	%	n	%	%	%
15–24	117	9.3	183	9.3	360	9.3	36.2	43.5
25–34	352	15.2	355	16.7	707	15.9	40.8	42.1
35–44	205	13.8	136	9.5	341	11.7	39.7	32.3
45–54	151	11.0	126	9.3	277	10.2	39.8	22.5
55–64	94	6.5	63	5.1	157	5.9	33.8	13.1
65–74	41	5.2	34	2.9	75	3.9	31.2	6.1
≥ 75	20	4.7	22	5.3	42	5.0	18.8	2.2
Total	1040	10.5	919	9.4	1959	9.9	36.6	28.4

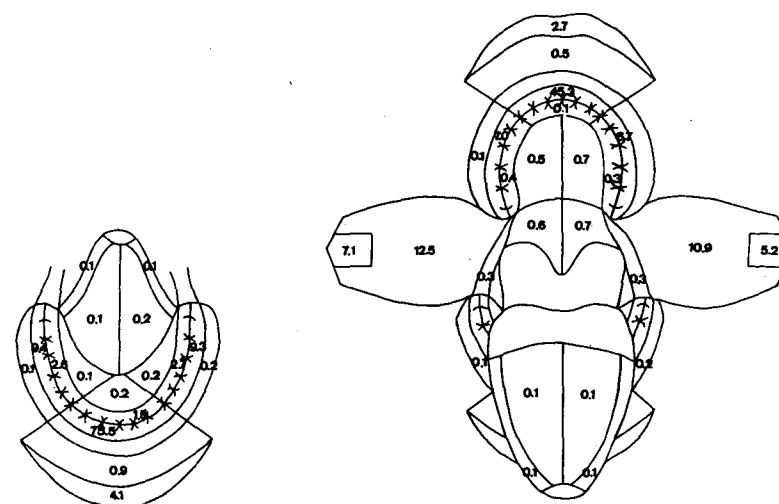


Fig. 1. Relative frequency (percent) of excessive oral melanin pigmentation in different locations among all individuals registered as having any oral melanin pigmentation.

Table 3

Number (*n*) of individuals with and prevalence (percent) of oral melanin pigmentation among individuals with different tobacco habits. Comparisons are made with individuals without any tobacco habit (difference of prevalence = *D*). Materials for comparisons matched according to age and sex. Standard error = *s.e.*, level of significance = *S*

Habit	<i>n</i>	%	<i>s.e.</i>	<i>D</i>	<i>S</i>
Any daily tobacco habit(s)	1541	18.9	0.53	15.9	***
Smoking	1429	21.5	0.61	18.4	***
Cigarette smoking	1159	21.9	0.68	18.9	***
Moderate cigarette smoking	780	19.4	0.73	16.4	***
Heavy cigarette smoking	379	29.9	1.59	26.8	***
Pipe smoking	127	16.8	1.50	13.8	***
Snuff dipping	42	4.7	0.79	1.6	n.s.
No tobacco habit	327	3.0	0.17		

tobacco users ($P > 0.05$). The correlation (*r*) between pigmentation and smoking for males and females calculated from values in different age groups (Table 1) were 0.82 and 0.83, respectively.

AMOUNT OF CIGARETTES

Even among individuals with a very low daily cigarette consumption (1–3 cigarettes a day) a significantly higher frequency of pigmentation, 9.3%, was found as compared to non-tobacco users ($P < 0.001$, Table 4). An additional increase of daily cigarette consumption further elevated the frequency. Thus, a very strong positive correlation was found between the daily

cigarette consumption and the frequency of pigmented individuals ($r = 0.98$, index of determination $r^2 = 0.97$, Fig. 2). Among moderate smokers females were significantly more often pigmented as compared to males, showing frequencies of 21.3% and 16.7%, respectively ($P < 0.001$).

DURATION OF SMOKING

Smoking for no more than 1 year yielded a considerably increased frequency of individuals showing oral melanin pigmentation. Among individuals having smoked 1 year the frequency was 14.6% as compared to 3.0% for non-tobacco users ($P < 0.001$). The frequency of pigmented

Table 4

Number of individuals with and frequency (percent) of oral melanin pigmentation among cigarette smokers. Distribution according to sex and daily cigarette consumption

No. of cigarettes a day	Average no. of cigarettes	Males		Females		Total	
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
1–3	2.6	14	8.0	18	10.7	32	9.3
4–7	5.6	42	13.5	101	15.8	143	15.1
8–11	9.7	81	15.6	217	21.8	298	19.7
12–15	14.2	119	22.4	188	28.5	307	25.8
> 15	21.3	235	29.1	144	33.1	379	30.5

Table 6

Number of individuals with and frequency (percent) of oral melanin pigmentation among ex-smokers. Distribution according to length of smoke-free period

Time elapsed after cessation of smoking		Pigmentation	
Months	Years	<i>n</i>	%
2–3		89	11.4
4–6		91	11.1
7–10		54	5.7
	1	293	5.1
	2	349	6.9
	3	233	3.5
	4–5	253	4.0
	6–10	269	3.0
	11–20	372	3.3
	21–30	113	3.6
	> 30	75	1.4

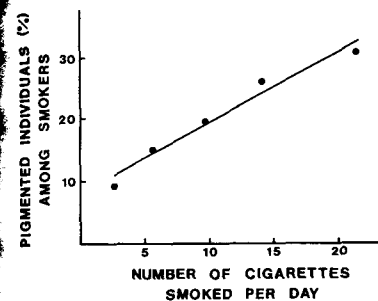


Fig. 2. Correlation between frequency (percent) of pigmented individuals among smokers and number of cigarettes consumed a day. The average value of smoked cigarettes was chosen for each sub-group. $r = 0.98$; $0.01 > P > 0.001$; $Y = 8.09 + 1.12X$; $t = 9.376$.

individuals only showed minor fluctuations until after 6 years of smoking when another prominent increase was observed reaching about 26% (Table 5).

CESSATION OF SMOKING

Among individuals who has stopped smoking an obvious decrease of pigmentation was observed. Three years after cessation the frequency of pigmentation was about 3%, i.e. similar to the prevalence among individuals not using tobacco. The prevalence among individuals with longer tobacco-free history was similarly low (Table 6).

Table 5

Frequency (percent) of oral melanin pigmentation. Distribution according to sex and duration of smoking

Duration years	Males	Females	Total
1	17.0	12.3	14.6
2	18.5	16.7	17.8
3	20.0	10.9	15.3
4–5	14.8	13.3	13.9
6–10	30.2	23.1	25.8
11–20	24.5	28.6	26.6
21–30	24.2	21.9	23.2

LOCATION OF PIGMENTATION RELATED TO TOBACCO HABITS

The pattern of pigmentation as regards location differed somewhat between individuals with different tobacco habits (Table 7). Among non-tobacco users females were significantly more often pigmented in the buccal mucosa than males, who more often showed pigmentation in the anterior labial alveolar process. Smokers were more frequently pigmented in all studied regions than individuals with no tobacco habit. Cigarette smoking males showed significantly more often pigmentation in all locations than pipe smokers (with the exception of the vermillion border) and to snuff dippers. Moderate cigarette smoking females were more frequently pigmented in the anterior labial alveolar process than males. Heavy cigarette smokers were significantly more often pigmented in all locations than moderate smokers. Pipe smokers showed pigmentation of the buccal mucosa significantly more often than moderate cigarette smoking males and snuff dippers. Snuff dippers were more often pigmented in the anterior labial alveolar process of the maxilla and the buccal mucosa than males not using tobacco.

Table 7

Frequency (percent) of oral melanin pigmentation distributed according to location and tobacco habits. Differences between groups with different tobacco habits are given as levels of significance

Habits	Total	Anterior labial alveolar process		Buccal or commissural mucosa	Vermillion border
		Maxilla	Mandible		
1. No habit, males	3.2	1.0	2.2	0.4	0.4
2. No habit, females	2.9	0.6	1.4	0.9	0.4
3. Smoking	21.4	11.3	17.4	3.2	0.9
4. Cigarette smoking, males	21.0	10.6	17.5	2.9	1.2
5. Cigarette smoking, females	23.1	12.9	19.1	3.0	0.8
6. Moderate cigarette smoking	19.5	10.2	16.3	2.5	0.8
7. Heavy cigarette smoking	30.5	17.3	25.2	4.5	1.4
8. Pipe smoking	16.6	8.3	13.2	6.0	0.8
9. Snuff dipping	4.7	1.9	2.9	1.4	0.5

Significance levels after comparison between groups					
Levels of significance					
Compared groups					
1 and 2	n.s.	*	**	**	n.s.
(1 + 2) and 3	***	***	***	***	***
1 and 9	*	*	n.s.	***	n.s.
3 and 9	***	***	***	***	n.s.
4 and 8	**	**	***	*	n.s.
4 and 9	***	***	***	***	*
6 and 7	***	***	***	***	*

Discussion

The prevalence of oral melanin pigmentation was 9.9%. Other epidemiologic investigations on Caucasians have shown similar figures. Among Caucasians in northern Sweden between 12.9% and 14.9% were pigmented (12), among white Londoners 5% (6) and among white South Americans 12.5% (14). The frequency among Gypsies was 33% (15) and among Asians about 40% (4). Significantly higher prevalences were found in other ethnic groups, e.g. among young Yemenite Jews 68% (8) and Australian aborigines 100% (16, 17). In the present study mainly Caucasian Swedes were examined but there was also a fraction of 6.8% foreign citizens. The main part of these, 5.2%, consisted of Finns. Only about 1% were South Europeans, mainly

Greeks, out of whom about 16% showed pigmentation. It was judged that they did not significantly influence the prevalence or frequency figures.

The frequency of oral melanin pigmentation shows variation by age (8). In Australian aborigines the frequency of gingival pigmentation decreased (17) and within various ethnic groups in London buccal pigmentation increased with age (6). In the present investigation the prevalence was highest in the younger age groups. This could partly be explained by the fact that among these, a higher proportion of tobacco smokers was observed. A contributing factor for the lower prevalences in the higher age groups may be the more frequent presence of dentures covering the mucosa (18). It is also

known that the activity of human skin melanocytes declines with age (19) and this could also be valid for melanocytes in the oral mucosa.

The present investigation confirms the findings by HEDIN (12) that tobacco smoking is the predominant etiologic factor for oral melanin pigmentation in Sweden. Presumably the discrepancies found between prevalence figures in different investigations may be explained partly by genetic differences in the populations but also to some extent by different tobacco habits. From the total prevalence figure of 21.5% of pigmented individuals among tobacco smokers in the present investigation, and the figure 3.0% among pigmented non-tobacco users, the prevalence of smokers' melanosis could be estimated to 18.5%. It could further be calculated that the overall frequency of smokers' melanosis in the total population was 6.8%. Of the population investigated 1.7% showed pigmentation that could not be linked to any actual tobacco habit. This pigmentation could to a minor extent comprise a remaining condition in ex-smokers as this group is included among non-tobacco users. Also other presently unknown external factors, such as influence of food and medical drugs, may play a role in the etiology of oral melanin pigmentation.

HEDIN (12) found a higher frequency of pigmented females than males among moderate smokers, raising the hypothesis of a synergism between female sex hormones and smoking. The present investigation supports this hypothesis. The higher frequency of smokers' melanosis found among females may reflect a physiologic reaction in the pigmentary system. This is also supported by the observation that it is mainly females who show exaggerated skin melanin pigmentation after medication with hydantoin, phenothiazines or levodopa (20). Further, female sex hormones are known to increase skin melanin pigmentation during menstruation, pregnancy and intake of oral contraceptives (21, 22).

The anterior labial alveolar mucosa was the most commonly pigmented region, in accordance with previous reports (3, 8, 12, 14). Buccal

melanin pigmentation was found in 1.7% in the present investigation, which could be compared to the findings of 5% in light skinned Caucasian Londoners (6). In the presently studied population the vermillion borders were more frequently pigmented than the tongue and palate in smokers as well as in non-smokers and this is in contrast to the findings by MONASH (3) and STEIGMANN (8). They found pigmentation of the lips to be very rare as compared to that of the tongue and palate. Enhanced melanin pigmentation in the palatal region is mentioned in reverse smokers (11) and found in smokers with serious lung diseases (23, 24).

Cigarette smokers were significantly more often pigmented in the anterior labial alveolar mucosa as compared to pipe smokers. This finding may indicate that the distribution of tobacco smoke in the oral cavity differs during cigarette and pipe smoking. Thus, the shaft of the pipe may distribute the pipe smoke preferably to the commissural and buccal mucosa. These regions were significantly more often pigmented in pipe smokers as compared to moderate cigarette smokers.

A different pattern of pigmentation was noticed among snuff dippers as compared to non-tobacco users. Snuff dippers were more frequently pigmented in the anterior labial alveolar mucosa of the maxilla and the buccal mucosa. However, it was remarkable that the mucosa in the labial fold corresponding to the site where the quid of snuff was regularly placed did not show any melanin pigmentation. Previous histologic studies of snuff lesions show various epithelial changes, but no melanin hyperpigmentation has been reported (25, 26). This difference between regions may be due to the differences in epithelial keratinization. Melanocytes also seemed to be much less sensitive to unburned tobacco than to tobacco smoke since even as low a daily consumption as 1-3 cigarettes significantly increased the frequency of pigmented individuals above the level found among snuff dippers.

The present study confirms that in Swedes oral melanin pigmentation is frequently found

among tobacco smokers. Thus, when an excessive oral melanin pigmentation is observed in a light skinned Caucasian who has not been a tobacco smoker for at least 3 years, alternative etiologic factors should be considered.

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Salivary gland function and changes in patients with oral lichen planus

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Lundström, I. M. C., Anneroth, K. G. B. & Bergstedt, H. F.: Salivary gland function and changes in patients with oral lichen planus. *Scand. J. Dent. Res.* 1982: 90: 443–458.

Abstract – Saliva analysis, sialography and histopathologic examination of labial salivary glands were performed on patients with oral lichen planus. Diseases connected with salivary gland function were also recorded. Saliva analysis regarding secretion rate, pH and buffer capacity in unstimulated and stimulated saliva was performed on 39 patients. 87% of the patients exhibited a low or very low unstimulated secretion rate, the mean value being 0.14 ml/min. The rate of stimulated saliva, pH and buffer capacity did not deviate from normal reference values. Sialographic examination was performed on 18 patients, corresponding to 36 major salivary glands. Radiologic changes were seen in 89% of the patients. Histopathologic examination was performed on 15 patients. Lymphocytic infiltration, acinar atrophy, fibrosis, fatty degeneration or ductal changes were observed in the minor glands of all patients. Different degrees of acinar atrophy were present in 93% of the patients. Lymphocytic infiltration was seen in 12 patients (80%) of whom three exhibited focal accumulation as in Sjögren's syndrome. Since decreased salivary secretion and symptoms of joint diseases and keratoconjunctivitis sicca were frequently present, over a third of the patients showed clinical signs comparable to those of Sjögren's syndrome. A high frequency of gastrointestinal and endocrine diseases was also recorded, which suggests that a general exo- and endocrine influence may be present in patients with oral lichen planus.

Key words: endocrine diseases; lichen planus; saliva; sialography; Sjögren's syndrome.

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Lichen planus is a disease that primarily appears to affect the epithelium of the mucous membranes and the skin (7, 44). Immunologic studies of the disease made in recent years point to the probable presence of a cell mediated immunologic response to antigenic changes in the basal cell layer (2, 21, 22, 39). The cause of this antigenic transformation in the epithelium is, however, unknown.

Patients with oral lichen planus (OLP) often present atrophic changes in the mucous membranes. According to ANDREASEN (3) clinically observable atrophic or atrophic-erosive lesions occurred in approximately 40% of a group of patients. Other investigators, however, have shown that these kinds of lesions are present in more than 60% of patients seeking treatment for OLP (42, 45). Even patients with the reticular or