

# Clinical symptoms and signs in sore throat patients with large colony variant $\beta$ -haemolytic streptococci groups C or G versus group A

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## ABSTRACT

### Background

The role of large colony streptococci groups C or G as pathogen agents in sore throat has been questioned.

### Aim

To analyse clinical features of patients with large colony streptococci groups C or G compared with patients with group A streptococci (GAS) and with negative cultures.

### Design of study

Prospective study of patients with sore throat.

### Setting

Two Norwegian general practices in Stokke and Kongsberg communities with 6500 patients.

### Method

Frequency of clinical features in the three patient categories including the four Centor criteria (fever, anterior cervical lymphadenopathy, tonsillar exudates, and lack of cough), degree of pain on swallowing, pharyngeal rubor, C-reactive protein (CRP) values, patient age between 3 and 14 years, and duration of symptoms before seeing the doctor. A logistic regression analysis to find independent predictors was performed.

### Results

Out of 306 patients with a sore throat, 244 were adults and 62 were children under 10 years old; 40% were men. One hundred and twenty-seven had GAS, 33 had streptococci groups C or G, and 146 had negative throat cultures. Forty-eight per cent of the GAS patients and 45% of the C or G patients met three or four of the Centor criteria. The logistic regression revealed that in patients with GAS considerable pain on swallowing, an age of 3–14 years and a duration of symptoms of  $\leq 3$  days or less were significantly associated with GAS infection in addition to the Centor criteria. The same results were found when all streptococci were analysed together, in addition elevated CRP was significant. In patients with streptococci group C or G an elevated CRP-value was significantly associated.

### Conclusion

Patients with tonsillitis caused by streptococcus groups C or G have, to a large extent, the same clinical picture as patients with GAS. Large colony streptococci groups C and G should be considered as throat pathogens in line with GAS.

### Keywords

bacteria; bacteriological culture; likelihood ratio; sensitivity and specificity; streptococcal infections; tonsillitis.

## INTRODUCTION

At least once a week a Norwegian GP with a list of 1500 patients is confronted with a patient with an acute sore throat.<sup>1</sup> The most pathogenic bacterial microorganism causing acute pharyngotonsillitis is group A streptococci (GAS),<sup>2</sup> because of its suppurative and non-suppurative sequelae and epidemiological potential. Penicillin has been the drug of choice for the treatment of group A  $\beta$ -haemolytic streptococcal pharyngitis for more than four decades because it moderately accelerates the resolution of symptoms and reduces the number of complications. However, the frequency of immunological complications have diminished during the last decade. The clinical significance of penicillin treatment is questionable, giving a reduction of symptoms of 1–2 days in patients with GAS.<sup>3,4</sup>

In Norwegian general practice the most common strategy of diagnosing sore throat with possible GAS infection is the use of an antigen detecting test based on the presence of two or three out of the four Centor criteria (fever, anterior cervical lymphadenopathy, tonsillar rubor and exudates, and lack of cough).<sup>5,6</sup> The antigen detecting test gives an answer to the presence of GAS within a few minutes and has high sensitivity and specificity.<sup>7</sup>

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## How this fits in

In national guidelines of management of sore throat in general practice the focus has been put on group A streptococci and the use of the four Centor criteria to sort out these patients. However, few studies have been made to evaluate whether large colony group streptococci C and G should be considered as pathogens. Patients with tonsillitis caused by large colony streptococcus groups C or G have to a large extent the same clinical picture as patients with GAS, and the frequency is one-fifth compared to patients with GAS. Large colony streptococci groups C and G should be considered as throat pathogens in line with GAS. Short duration of symptoms, considerable pain on swallowing, an age of 3–14 years and elevated CRP-value are of additional value in diagnosing streptococcal tonsillitis.

Few previous studies have analysed the clinical picture of tonsillitis caused by large colony streptococci belonging to groups C and G,<sup>8</sup> which also have been considered to be pathogenic.<sup>9</sup> In a US study on college students, Turner analysed clinical features in patients with tonsillitis caused by group C streptococci and concluded that large colony group C should be regarded as pathogenic while groupable streptococci belonging to the *anginosus* subgroup should be regarded as part of the normal flora.<sup>10</sup> Zwart found in his study that streptococci group C or G with a high colony count had a significantly shorter duration of illness with treatment with penicillin V than with placebo,<sup>4</sup> although the mean difference of 1 day is of questionable clinical significance. The objectives of our study were to:

- analyse the clinical features in patients with sore throats with streptococci groups C or G compared to patients with GAS and with negative cultures;
- analyse the distribution of Centor criteria in the three categories of patients; and
- analyse whether other clinical symptoms, signs and blood tests could be of additional diagnostic value, based on presence of Centor criteria in a logistic regression.

### METHOD

This study is part of a sore throat study carried out in two Norwegian health centres, one in Stokke community with four participating doctors, and one in

the Kongsberg community with one participating doctor. The patient lists of the five doctors included a total of 6500 patients. Patients with a sore throat seeking a doctor were recruited if they had symptoms for less than 7 days but were excluded if they had received an antibiotic course during the past 2 weeks.

In the first consultation the patients were first subjected to a clinical investigation including evaluation according to the Centor criteria in addition to background data of age, sex and duration of symptoms prior to consultation. The doctors involved were trained in the use of the Centor criteria. However, no test of interobserver variation was performed. Other clinical clues with possible relation to streptococcal infection were recorded. The degree of pain at swallowing was recorded on a 3-point scale (little, moderate, considerable pain). We also recorded presence of rubor in pharynx and a C-reactive protein (CRP)-test was performed.

### Tonsillopharyngeal samples

Tonsillopharyngeal swabs were taken from the included patients at their first visit. Two identical swabs placed in parallel were taken simultaneously under the guidance of vision. The tonsillar region, including the crypts, and the posterior pharyngeal wall, were scrubbed vigorously. One swab was placed into a tube of modified Stuarts transport medium and mailed to the National Institute of Public Health (NIPH) for bacteriological typing and subgrouping; the other was processed and interpreted according to the instructions given by the manufacturer of the antigen detecting test.

For all media used, the plates were incubated overnight at 35°C, and inspected the next day; followed by another 24 hours at room temperature before final reading. All colonies suspected of being  $\beta$ -haemolytic streptococci were further spread to pure cultures and serogrouped. To find all patients with GAS and other streptococci, we used two cultures; methods are described elsewhere.<sup>7</sup>

### Serogrouping and typing

GAS isolates were identified by standard methods and serogrouped with Prolex™ Blue Streptococcal Grouping Kit (A, B, C, D, F, G) (Pro-Lab Diagnostics, Richmond Hill, Ontario, Canada). Isolates were frozen at -70°C in Greaves' medium until typed by anti-T sera from Sevapharma (Prague, Czech Republic) and examined for opacity factor.<sup>11,12</sup> The classification of pathogenic streptococci was based on all GAS and large colony groups C or G.<sup>8</sup>

In the statistical analysis  $\chi^2$  and Student's *t*-tests were used. In the evaluation of the clinical clues by bacteriological results, we calculated sensitivities, specificities, and likelihood ratios. We also used a logistic regression analysis to find whether other

**Table 1. Baseline characteristics of 306 patients with sore throat by streptococcal culture, southern Norway 2000–2002.**

	GAS <i>n</i> = 127	C or G <i>n</i> = 33	Culture -ve <i>n</i> = 146	Total <i>n</i> = 306	<i>P</i> -value
Mean age (years) (95% CI)	21.5 (19.0 to 23.9)	25.2 (20.6 to 29.7)	5.8 (23.2 to 28.4)	23.9 (22.2 to 25.6)	0.02 <sup>a</sup>
Number of males (%)	48 (38)	13 (39)	62 (43)	123 (40)	ns
Duration of complaints in days (95% CI)	3.0 (2.7 to 3.3)	3.1 (2.4 to 3.7)	3.5 (3.2 to 3.8)	3.2 (3.0 to 3.4)	0.008 <sup>a</sup>
Positive ADT GAS test (%)	123 (97)	1 (3)	9 (6)	133 (43)	
Mean CRP-values (95% CI)	50 (41 to 59)	43 (32 to 53)	34 (29 to 40)	41 (37 to 46)	0.001 <sup>a</sup>

<sup>a</sup>GAS versus group with no bacteria. GAS = group A streptococci. ADT = antigen detecting test.

**Table 2. Number of patients with clinical features with streptococcal culture as reference standards in 306 patients with sore throat by streptococcal culture, southern Norway 2000–2002.**

Clinical features	GAS	C or G	Culture -ve	Total	GAS			C or G		
	n = 127 n (%)	n = 33 n (%)	n = 146 n (%)	n = 306 n (%)	Sens	Spec	LR	Sens	Spec	LR
Centor criteria:										
Cervical adenitis	114 (90) <sup>a</sup>	27 (82)	101 (70)	242 (80)	0.90	0.30	1.3	0.82	0.30	1.2
Absence of cough	96 (76) <sup>a</sup>	21 (64)	67 (46)	184 (60)	0.76	0.54	1.7	0.64	0.54	1.3
Reported fever >38.0°C	67 (53)	20 (61)	69 (48)	156 (52)	0.53	0.52	1.1	0.61	0.52	1.3
Tonsillar exudate	32 (25)	8 (24)	48 (34)	88 (29)	0.25	0.66	0.8	0.24	0.66	0.8
Considerable pain on swallowing	70 (57) <sup>a</sup>	12 (36)	50 (35)	132 (44)	0.57	0.65	1.6	0.36	0.65	1.0
Rubor in pharynx	112 (88) <sup>a</sup>	26 (79)	106 (75)	244 (81)	0.88	0.25	1.2	0.79	0.25	1.1
CRP value:										
>25 mg/l	68 (53)	22 (67) <sup>a</sup>	60 (41)	150 (49)	0.53	0.59	1.3	0.67	0.59	1.6
>50 mg/l	45 (35)	11 (33)	29 (20)	85 (28)	0.35	0.80	1.8	0.33	0.80	1.7

<sup>a</sup>P<0.05 in bivariate analysis of GAS versus group with no bacteria. GAS = group A streptococci. Sens = sensitivity. Spec = specificity. LR = likelihood ratio. CRP = C-reactive protein.

clinical clues than the Centor criteria were independent predictors of presence of GAS or streptococci groups C or G. The level of significance was set to 0.05.

## RESULTS

Of all the eligible patients with a sore throat in the time period, 90% were willing to participate. Patients were recruited from April 2000 until June 2002. In the summer holidays from the middle of June until the middle of August patients were not recruited due to lack of laboratory availability.

Three hundred and ten patients were recruited to the study, but in four patients the bacteriological samples were impossible to interpret. In the 306 patients that were evaluated, 244 were adults and 62 were children under 10 years of age. The mean age was 23.9 years (standard deviation = 15.0 years) and 123 (40%) were men. One hundred and twenty-seven patients had group A streptococci in the culture, 21 grew group G and 12 grew group C streptococci, and the remaining 146 had negative streptococcal cultures.

Table 1 gives background data of the patients with GAS, group C or G and negative cultures, including age, sex, duration of complaints before seeing the doctor and results of antigen detecting test and CRP-

test done in the office. The patients with GAS were significantly younger than the two other categories. As previously demonstrated the antigen detecting test had a sensitivity of 0.97 and a specificity of 0.95.<sup>7</sup> The CRP-values were significantly higher in the GAS-patients compared to the non-streptococcal patients, whereas the mean values were higher also in the C or G patients, not reaching significant difference.

Table 2 gives the sensitivity, specificity and likelihood ratio (LR) of the four Centor criteria and other relevant clinical clues for the GAS and the C or G category compared to the patients with a negative culture. Among the Centor criteria cervical adenitis and absence of cough had the highest sensitivity and LR for both the GAS-category and the C or G-category. Fever and tonsillar exudate were not significantly different in the streptococcal categories compared to the category with negative culture. The LR equals the proportion between a positive finding in the streptococci category and in the category with negative culture.

Among the other clinical features considerable pain on swallowing and rubor in the pharynx were significantly more frequent in the GAS category compared to the category with negative culture. A CRP value above 25 mg/l was significantly more frequent in

**Table 3. Number of Centor criteria by streptococcal groups in 306 patients with sore throat by streptococcal culture, southern Norway 2000–2002.**

Clinical features	GAS	C or G	Culture -ve	Total	GAS			C or G		
	n = 127 n (%)	n = 33 n (%)	n = 146 n (%)	n = 306 n (%)	Sens	Spec	LR	Sens	Spec	LR
Four Centor criteria	19 (15)	4 (12)	14 (10)	37 (12)	0.15	0.90	1.5	0.12	0.90	1.2
Three Centor criteria	42 (33)	11 (33)	33 (23)	86 (29)	0.33	0.77	1.4	0.33	0.77	1.4
Two Centor criteria	46 (37)	10 (30)	46 (33)	102 (34)	0.37	0.67	1.1	0.30	0.67	0.9
One Centor criterion	15 (12)	7 (21)	31 (22)	53 (12)	0.12	0.78	0.6	0.21	0.78	1.0
Zero Centor criteria	4 (3)	1 (3)	17 (12)	22 (7)	0.03	0.88	0.3	0.03	0.88	0.3
Three or more Centor criteria	61 (48) <sup>a</sup>	15 (45)	47 (33)	123 (41)	0.48	0.67	1.5	0.45	0.67	1.4
Two or more Centor criteria	107 (85) <sup>a</sup>	25 (75)	93 (66)	225 (75)	0.85	0.34	1.3	0.75	0.34	1.1

<sup>a</sup>P<0.05 in bivariate analysis of GAS vs group with no bacteria. GAS = group A streptococci. Sens = sensitivity. Spec = specificity. LR = likelihood ratio.

**Table 4. Logistic regression analysis of diagnostic value of clinical features and blood tests in the diagnosis of GAS and C or G streptococci in addition to the presence of Centor criteria in 306 patients with sore throat by streptococcal culture, southern Norway 2000-2002.**

Clinical feature	GAS			C or G streptococci			All streptococci		
	OR	(95% CI)	P-value	OR	(95% CI)	P-value	OR	(95% CI)	P-value
Four Centor criteria	2.6	(0.7 to 10.6)	0.17	3.0	(0.3 to 31.7)	0.36	2.3	(0.6 to 8.5)	0.23
Three Centor criteria	3.5	(1.0 to 12.3)	0.04	3.7	(0.4 to 32.6)	0.23	3.5	(1.1 to 11.2)	0.03
Two Centor criteria	3.0	(0.9 to 10.1)	0.07	3.2	(0.4 to 27.2)	0.29	2.8	(0.9 to 8.4)	0.07
One Centor criterion	1.9	(0.5 to 7.0)	0.34	3.5	(0.4 to 31.7)	0.26	2.0	(0.6 to 6.5)	0.26
Zero Centor criteria (reference)	1.0			1.0			1.0		
Rubor in pharynx	ns			ns			ns		
Considerable pain on swallowing	2.5	(1.4 to 4.5)	0.003	ns			1.8	(1.0 to 3.1)	0.04
Mild/moderate pain (reference)	1.0						1.0		
Duration of symptoms									
<4days	2.0	(1.1 to 3.5)	0.02	ns			1.7	(0.9 to 2.9)	0.06
≥4 days (reference)	1.0						1.0		
Age 3-14 years	2.6	(1.4 to 5.0)	0.003	ns			2.1	(1.1 to 3.9)	0.02
Other ages (reference)	1.0						1.0		
CRP >25 mg/l	ns			2.5	(0.9 to 6.6)	0.07	1.1	(0.5 to 2.1)	0.84
CRP >50 mg/l				2.8	(1.0 to 7.5)	0.04	2.0	(1.0 to 3.8)	0.04
CRP <25 mg/l (reference)				1.0			1.0		

OR = Odds ratio. CRP = C-reactive protein. GAS = group A streptococci.

the C or G category compared to the negative category.

Table 3 gives the frequency of the number of Centor criteria summated in the three categories. Patients with four, three and two Centor criteria were more frequent in the streptococcal categories compared to the culture negative category, the difference being significant in the GAS-category when patients with four, three and two criteria are summated. In patients with four, three or more, two or more and three or two Centor criteria we found a 62%, 62%, 59% and 58% chance of having either streptococci group A or group C or G, respectively. With one or zero criteria present, we found a 43% and a 25% chance of having a streptococcal infection, respectively. There was no significant difference between the proportion of Centor-criteria in patients with low and high colony count of streptococci.

In Table 4 the results of a logistic regression analysis are presented, with each of the streptococcal patient categories compared to the negative category. We found that Centor criteria were significantly associated in the GAS-category while considerable pain on swallowing, having an age between 3 and 14 years, and duration of complaints before seeing a doctor of 3 days or less also were significantly associated. The other clinical features, such as pharyngeal rubor and CRP values that were significant in the bivariate analysis, were not significantly associated.

In the C or G category the Centor criteria did not reach significance, but had an odds ratio of the same size as the GAS-category. In this analysis a CRP value above 50 mg/l was significantly associated. When both the streptococcal categories summarised were compared to the category with negative culture we found that the following features were significantly

associated: Centor criteria three or four, elevated CRP values, considerable pain on swallowing, low duration of symptoms, and age 3-14 years.

## DISCUSSION

### Summary of main findings

The main finding of this study is the similarity in clinical features between patients with streptococci group A and group C or G. The frequency of each of the four Centor criteria is generally of the same proportion. When the Centor criteria were summated, we found that 48% of the patients with GAS and 45% of the patients with group C or G met three or four of the criteria. Furthermore, we found that other clinical features also were significantly associated with the presence of streptococci even when added to the Centor criteria. We found that considerable pain on swallowing, having an age between 3 and 14 years and duration of complaints before seeing a doctor of 3 days, were significantly associated with presence of GAS, and that CRP >25 mg/l was significantly associated with presence of streptococci group C or G.

### Strengths and limitations of the study

One strength of the study is our setting with patients in primary care seeking a doctor, with sore throat as their main reason for the encounter and with an illness duration of less than 7 days, being the clinical setting which is closest to daily general practice. With four or three Centor criteria present, the chance of finding a streptococcal infection was 62%, thus 38% of patients with these criteria present had another infection. Although we do not have any data for this, we assume that these represent viral infections, such

as mononucleosis, adenovirus or other viruses. In a previous study we found that the antigen detecting test had a sensitivity of 97% and specificity of 95% of detecting GAS.<sup>7</sup> This may indicate that the antigen detecting test is of additional value in finding GAS compared to the use of Centor criteria alone. It can be questioned whether the use of Centor criteria should be the basis of the use of antigen detecting test, as is the present Norwegian recommendation.<sup>5</sup> It is also important to remember that the patient can be a possible carrier of GAS and that the sore throat is caused by a viral infection.

### Comparisons with existing literature

Few previous studies have analysed the clinical picture of tonsillitis caused by large colony group C and G streptococci. Our findings are in line with the US study on college students, where Turner analysed clinical features in patients with tonsillitis caused by large colony group C streptococci.<sup>10</sup> Furthermore our findings are also in line with findings of Meland *et al* who analysed the clinical features of the same groups of streptococci summarised, giving similar results.<sup>9</sup>

Our findings raise the question of the validity of the Centor criteria, which has been questioned previously by Little, especially in children.<sup>13,14</sup> We found that among the four Centor-criteria, only cervical adenitis and absence of cough were significantly more frequent in the GAS category compared to the category with negative culture. Reported fever was of the same proportion in all three categories, and tonsillar exudate was, in fact, somewhat more frequent in the category with negative culture, although not significantly different. One of the reasons for this may be difference in study populations between the various studies that have been performed.<sup>2,6,9</sup>

Some studies have argued that being aged 3–14 years old should be added as a fifth Centor criteria.<sup>15</sup> Our findings are in line with those of Meland *et al* who found that in a logistic regression analysis only a lack of cough, swollen lymph nodes and an age >4 years were significantly associated with streptococcal tonsillitis.<sup>9</sup> In other studies an elevated CRP-value has been found to be of additional value in the clinical diagnosis of GAS.<sup>16,17</sup> Short duration of symptoms has previously been shown to be of diagnostic value.<sup>18,19</sup> We have not found any other studies evaluating the presence of considerable pain on swallowing.

### Implications for future research

In this study we used throat culture as a reference standard for presence of infection. A different reference standard could be serological response to infection which probably is more valid to exclude carriers. Another important topic would be to trace out which patients with streptococcal infections receive the most

benefit from penicillin treatment.

Our study has demonstrated that, to a large extent, patients with tonsillitis caused by group C or G streptococci demonstrate the same clinical picture as patients with GAS. The frequency of patients with group C or G streptococci is around one-fifth compared to patients with GAS and this has also been shown in other studies.<sup>4,9</sup> Therefore, group C or G streptococci are a common cause of tonsillitis. Since Zwart *et al* have demonstrated a significant effect of treatment of C or G streptococci with penicillin V, we suggest that large colony streptococci groups C and G should be considered as throat pathogens in line with GAS.

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### Ethical committee

The study was approved by the regional ethical committee (S-00038 February 2000)

### Conflict of interest

None

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### REFERENCES

- Melbye H. Lungs and airway diseases. In: Hunskaar S, (ed). *General practice*. Oslo: Gyldendal Akademisk, 2003: 441–469.
- Dagnelie CF, Bartelink ML, van der Graaf Y, *et al*. Towards a better diagnosis of throat infections (with group A beta-haemolytic streptococcus) in general practice. *Br J Gen Pract* 1998; **48**(427): 959–962.
- Del Mar CB, Glasziou PR, Spinks AB. Antibiotics for sore throat (review). *Cochrane Database Syst Rev* 2004(2): CD000023.
- Zwart S, Sachs AP, Ruijs GJ, *et al*. Penicillin for acute sore throat: randomised double blind trial of seven days versus three days treatment or placebo in adults. *BMJ* 2000; **320**(7228): 150–154.
- Berild D (ed). *Antibiotics in general practice — national guidelines*. Oslo: National Board of Health, 2000.
- Centor RM, Witherspoon JM, Dalton HP, *et al*. The diagnosis of strep throat in adults in the emergency room. *Med Decis Making* 1981; **1**(3): 239–246.
- Lindbaek M, Høiby EA, Lermark G, *et al*. Which is the best method to trace group A streptococci in sore throat patients: culture or GAS antigen test? *Scand J Prim Health Care* 2004; **22**: 233–238.
- Ruoff KL, Whiley RA, Beighton D. *Streptococcus*. In: Murray PR, Baron EJ, Jorgensen JH, Tenover FC, Tenover FC, (eds). *Manual of clinical microbiology*. Washington DC: American Society of Microbiology, 2003: 405–421.
- Meland E, Digraanes A, Skjaerven R. Assessment of clinical features predicting streptococcal pharyngitis. *Scand J Infect Dis* 1993; **25**(2): 177–183.
- Turner JC, Hayden FG, Lobo MC, *et al*. Epidemiologic evidence for Lancefield group C beta-hemolytic streptococci as a cause of exudative pharyngitis in college students. *J Clin Microbiol* 1997; **35**(1): 1–4.
- Martin PR, Hoiby EA. Streptococcal serogroup A epidemic in Norway 1987–1988. *Scand J Infect Dis* 1990; **22**(4): 421–429.
- Rehder CD, Johnson DR, Kaplan EL. Comparison of methods for obtaining serum opacity factor from group A streptococci. *J Clin Microbiol* 1995; **33**(11): 2963–2967.
- Zwart S, Rovers MM, de Melker RA, Hoes AW. Penicillin for acute sore throat in children: randomised, double blind trial. *BMJ* 2003; **327**(7427): 1324.
- Little P. Penicillin for acute sore throat in children: randomised, double blind trial. Commentary: More valid criteria may be needed. *BMJ* 2003; **327**(7427): 1327–1328.
- McIsaac WJ, Goel V, To T, Low DE. The validity of a sore throat score in family practice. *CMAJ* 2000; **163**(7): 811–815.
- Gulich MS, Matschiner A, Gluck R, Zeitler HP. Improving diagnostic accuracy of bacterial pharyngitis by near patient measurement of C-reactive protein (CRP). *Br J Gen Pract* 1999; **49**(439): 119–121.
- Hjortdahl P, Melbye H. Does near-to-patient testing contribute to the diagnosis of streptococcal pharyngitis in adults? *Scand J Prim Health Care* 1994; **12**(2): 70–6.
- Kljakovic M. Sore throat presentation and management in general practice. *N Z Med J* 1993; **106**(963): 381–383.
- McIsaac WJ, White D, Tannenbaum D, Low DE. A clinical score to reduce unnecessary antibiotic use in patients with sore throat. *CMAJ* 1998; **158**(1): 75–83.