

PHONiatrics

Correlation between female sex and allergy was significant in patients presenting with dysphonia

Associazione tra sesso ed allergia in pazienti affetti da disfonia

M. LAURIELLO, A.M. ANGELONE¹, L. DI RIENZO BUSINCO², D. PASSALI³, L.M. BELLUSSI³, F.M. PASSALI⁴

Department of Internal Medicine and Public Health, University of L'Aquila; ¹ Experimental Medicine Department, University of L'Aquila; ² ENT Department, ASL C Rome; ³ ENT Clinic, University of Siena; ⁴ ENT Department, "Tor Vergata University", Rome, Italy

SUMMARY

Aim of the present study was to investigate the prevalence of allergy in patients affected by both organic and/or functional vocal fold disorders. The secondary aim was to assess the correlation between sex and allergy in dysphonic patients. A retrospective chart review was performed on dysphonic patients. A total of 76 patients underwent fiberoptic endoscopy to assess the objective picture. Logistic regression analyses have been conducted to assess the association between sex and the outcome variables. The laryngoscopic examination revealed the presence of poor glottic closure in 32.9%, hyperkinesias in 11.8%, redness in 11.84%, polyps in 5.3%, oedema in 3.95%, vocal fold hypertrophy in 5.3%, nodules in 42.1%, cordectomy in 2.6%. Allergic rhinitis was present in 56.6%, milk intolerance in 13.2%, asthma in 9.2%, atopic dermatitis in 3.9%, drugs intolerance in 11.8%. A total of 76.32% patients presenting with dysphonia were allergic. A statistically significant association was found between female sex and presence of allergy. In conclusion, allergy testing should be performed routinely on female professional voice users. Mild respiratory disorders must be taken into serious consideration in female professional voice users, who may primarily complain of vocal dysfunction rather than upper and lower respiratory diseases.

KEY WORDS: Allergy • Dysphonia

RIASSUNTO

Il presente studio si è proposto di indagare la prevalenza di allergie in pazienti affetti da disturbi vocali di natura organica e/o funzionale. L'obiettivo secondario è stato quello di valutare la correlazione tra sesso ed allergia nei pazienti disfonici. È stata eseguita una revisione retrospettiva delle cartelle cliniche di 76 pazienti disfonici sottoposti a fibroscopia per la valutazione del quadro obiettivo laringeo. Sui dati raccolti è stata condotta un'analisi statistica per valutare l'associazione tra sesso, età, allergia e disfonia. L'esame laringoscopico ha evidenziato la presenza di insufficienza glottica nel 32,9% dei soggetti, ipercinesia nell'11,8%, eritema nell'11,84%, presenza di polipi nel 5,3%, edema nel 3,95%, ipertrofia delle corde vocali nel 5,3%, noduli nel 42,1%. La rinite allergica era presente nel 56,6% dei soggetti esaminati, l'intolleranza al latte nel 13,2%, l'asma nel 9,2%, la dermatite atopica nel 3,9%, l'intolleranza a farmaci nell'11,8%. Complessivamente il 76,32% dei pazienti affetti da disfonia erano allergici. Un'associazione statisticamente significativa è stata inoltre rilevata tra sesso femminile e presenza di allergia. In conclusione nei professionisti della voce di sesso femminile dovrebbero essere presi in seria considerazione anche lievi disturbi respiratori: questi soggetti infatti possono accusare disturbi vocali prima di manifestare patologie a carico dell'apparato respiratorio superiore o inferiore. Per lo stesso motivo, un'indagine allergologica dovrebbe essere eseguita di routine in tutti i professionisti della voce di sesso femminile.

PAROLE CHIAVE: Allergia • Disfonia

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Introduction

The troubles caused by allergies are often compounded by the multiplicity of complaints involved ¹. Among common symptoms, such as rhinitis, middle ear effusion, asthma, vocal quality disorders had been found frequently in association with respiratory allergy ². In a population of 80 allergic children and young adults (age range 8 to 23 years), Baker et al. ¹ found vocal quality disorders (hoarseness, breathiness, low vocal intensity) in 44.75% of the cases. This percentage was about eight times greater than that

(6%) found in mass screening in the same metropolitan area. The Authors suggested that chronic allergic rhinosinusitis may predispose a child to recurrent hoarseness and eventual development of a benign lesion in the true vocal folds.

Occasionally, patients report that they became dysphonic when they were exposed to various external irritants or pollutants in the air: generally the complaints are dryness, harshness, tickling and hoarseness ³.

A medical approach for functional voice disorders had been proposed in a recent prospective randomised pilot

study⁴. A very detailed anamnesis and systematic objective routine analyses led to the discovery of “micro-organic disorders” caused by reflux, infection, allergy or environmental irritants. The medical treatment of these pathological conditions resolved also the functional voice disorders. According to the Authors the reason was that the mucosal swelling/dysfunction of the vocal folds was secondary.

The aim of the present study was to establish whether a correlation exists between the sex and the presence of allergy in dysphonic patients.

Methods

A retrospective chart review was performed of all patients seen in the Voice Centre of the ENT Department ASL RM C and in the ENT Clinic, University of Siena, between September 2006 and September 2007.

The patients (a total of 90) come to the centres for vocal training because of symptoms including hoarseness, vocal fatigue, pitch break, and loss of vocal range.

The retrospective study was carried out excluding not only those cases for whom the anamnesis was positive for smoking habits, but also women already in menopause.

A total of 76 patients (13 male, 63 female) were included in the study. Age range 14-80 years (mean 34.3 years).

The patients underwent fiberoptic endoscopy, aimed at assessing the exact state of the larynx. Acoustic analysis of the voice was performed in 9% of the patients enrolled, albeit the results are not reported in this study as they were not statistically significant.

Statistics

The data collected have been very carefully assessed and then recorded on a magnetic support at the Department of Internal Medicine and Public Health of the University of L'Aquila, and elaborated using the STATA 8 programme. Therefore, logistic regression analyses have been carried out to assess the association between sex and the outcome variables after adjusting for age, these being considered potential confounders.

The associations have been expressed as Odds Ratio (OR) with a confidence interval (CI) reaching 95%.

Results

The laryngoscopic examination revealed the presence of muscle tension dysphonia in 25 patients (32.9%), hyperkinesia in 9 (11.8%), redness in 9 (11.84%), polyps in 4 (5.3%), oedema in 3 (3.95%), vocal fold hypertrophy in 4 (5.3%), nodules in 32 (42.1%), cordectomy in 2 (2.6%) (Table I). Otorhinolaryngologic evaluation is summarized in Table II together with other disorders. A pale nasal mucosa was observed in 2 subjects (2.6%), nasal secretion in 6 (7.9%), turbinates hypertrophy in 24 (31.6%), pharyn-

Table I. Laryngological assessment (the total percentage is higher than 100 because some subjects are suffering from more than one disease).

	%	N
Poor glottic closure	32.9	25
Hyperkinesia	11.8	9
Vocal fold redness	11.8	9
Polyps	5.3	4
Vocal fold oedema	3.9	3
Vocal fold hypertrophy	5.3	4
Nodules	42.1	32
Cordectomy	2.6	2

Table II. Otolaryngologic assessment.

	%	N
Pale nasal mucosa	2.6	2
Nasal secretion	7.9	6
Hypertrophy of turbinates	31.6	24
Pharyngitis	2.6	2
Gastro-oesophageal reflux	19.7	15
Mood disorders	5.3	4
Others	5.3	4

gitis in 2 (2.6%), gastro-oesophageal reflux in 15 (19.7%), as assessed by 24hr intraluminal oesophageal pH monitoring; furthermore mood disorders were reported in 4 cases (5.3%), other diseases in 4 (5.3%).

Pertinent medical history is summarized in Table III: allergic rhinitis was present in 43 patients (56.6%), milk intolerance in 10 (13.2%), asthma in 7 (9.2%), atopic dermatitis in 3 (3.9%), drugs (aspirin/ FANS and penicillin/derivates) allergy in 9 (11.8%).

The percentages of allergic and not allergic subjects are shown in Figure 1.

Subjects suffering from one, two or three kinds of allergy were, respectively, 44 (57.89%), 13 (17.11%), and 1

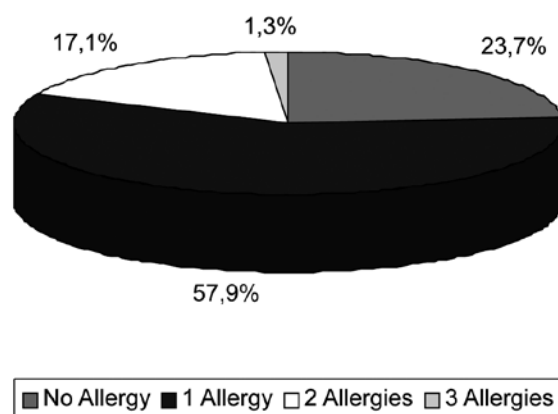


Fig. 1. Percentages of allergic and non allergic subjects.

Table III. Pertinent medical history of allergy.

	%	N
Allergic rhinitis	56.6	43
Milk intolerance	13.2	10
Asthma	9.2	7
Atopic dermatitis	3.9	3
Intolerance to drugs	11.8	9

(1.32%). A total of 58 patients (76.32%) affected by dysphonia were allergic.

As far as concerns the correlation between sex and allergy, manifestations of allergic disorders have been found in 6 males and 52 females. The application of Pearson's chi square revealed a significant association between female sex and presence of allergy in patients suffering from dysphonia (Pearson's chi square = 7.89, $P = 0.005$).

Furthermore, sex was considered a "risk factor" and was associated with each pathological condition detected. A statistically significant association has been pointed out between female sex and presence of allergy (OR 5.51; CI: 1.55 - 19.63). In the same subjects female sex status resulted a "protective factor" against gastro-oesophageal reflux (OR 0.12; CI: 0.03 - 0.46) (Table IV).

The same statistical analysis had been carried out referring to each above-mentioned disease. The results were not shown in the Tables because the respective associations were not significant.

Discussion

Together with other organs of the supraglottic vocal tract⁵, the nose is responsible for vocal quality, timbre and the perceived character of all speech sounds⁶.

A recent study focusing on acoustic estimation of the voice when incorrect resonance function of the nose takes place, showed that in patients (aged from 5 to 15 years) with seasonal allergic rhinitis, presenting also bronchial asthma, the mean Jitter and Shimmer values were higher than in the control group, but the values did not show a statistically significant difference⁷.

Table IV. Associations (Odds Ratio-OR confidence interval up to 95%) between some diseases and sex (* Statistically significant differences OR adjusted for age).

Allergy		
Sex	OR	(95% CI)
Male	1	
Female	5.51	(1.55-19.63)*
Reflux		
Male	1	
Female	0.12	(0.03-0.46)*

The most common acute vocal fold injuries are submucosal haemorrhage and mucosal tears.

Our laryngoscopic examination revealed the presence of muscle tension dysphonia in 25 patients (32.9%), hyperkinesia in 9 (11.8%), redness in 9 (11.84%), polyps in 4 (5.3%), oedema in 3 (3.95%), vocal fold hypertrophy in 4 (5.3%), nodules in 32 (42.1%), cordectomy in 2 (2.6%).

Most patients suffering from vocal fold haemorrhages have concurrent reflux, asthma or allergy⁵. Chronic laryngeal disorders include vocal nodules, polyps and vocal fold oedema. The latter can result from chronic inflammation, environmental allergy, inhaled irritants, poor vocal technique, or any combination of these factors.

In our study, a pale nasal mucosa was observed in 2 subjects (2.6%), nasal secretion in 6 (7.9%), hypertrophy of the turbinates in 24 (31.6%), pharyngitis in 2 (2.6%), gastro-oesophageal reflux in 15 (19.7%), as assessed by 24-hour intra-luminal oesophageal pH monitoring.

The larynx is seldom mentioned in the reports on allergy of the upper and lower respiratory system. In spite of this lack of information, allergic reactions of the larynx exist, but they are not usually diagnosed or are misdiagnosed: only in the case of anaphylactic reaction does the severe impairment of the airways draw the attention to the relationship between allergy and larynx. The existence of a direct allergic response in the larynx has meaningful implications for the diagnosis and treatment of dysphonia⁸. A direct demonstration of laryngeal allergy has been obtained by applying drops of an antigen solution to the arytenoid mucosa and then carrying out a cytodiagnostic study of the site. The latter demonstrated the degranulation of the plasma cells⁹.

The presence of mast cells in the larynx had been demonstrated in the human embryo, although the mast cell count in the larynx was lower than in the trachea and bronchi¹⁰.

In the study carried out by Haapanen³, the provocation of voice disorders had been performed by spraying the allergen onto the posterior wall of the pharynx in order not to elicit the laryngeal protective reflex: the hypersensitivity to house dust proved to induce laryngeal dysfunction. The latter had been demonstrated by indirect laryngoscopy and by voice recordings, analyzed with a Sonagraph or with a real-time spectrograph.

Immediate allergic laryngitis by pollen and mites had been reported by Buczylo et al.¹¹: 34 allergic patients, revealed by positive skin prick tests, confirmed a change in vocal cord status after natural provocation.

Takeda et al.¹² proposed five features as diagnostic criteria for laryngeal allergy:

History: past or family history of allergic disease.

Symptoms: cough, foreign body sensation in the throat and sputum.

Local findings: oedema and pale arythenoid mucosa.

Laboratory data: eosinophilia in the peripheral blood, positive intradermal reactions.

Treatment: efficacy of anti-allergic and antihistamine agents.

Foods, bee sting, drugs, and inhalants had already been mentioned since the first decades of the past century as factors involved in the pathogenesis of chronic laryngitis and oedema of the vocal folds¹³⁻¹⁷.

According to Williams¹⁸, the mechanism of allergic laryngitis is primarily oedema formation in the entire larynx or in specific portions such as arytenoids or vocal folds. The oedema of the contact surface of the true vocal cords produces hoarseness, which is a quality of the voice that is harsh, discordant and of low pitch. In fact, the oedema changes the size and the rigidity of the vibrating mass, interfering with the pitch and the proprioceptive sensations through which the voice is controlled during speaking and, more important, during singing.

The main aetiological factors are inhalants (house dust, moulds, animal danders, feathers) and pollens. Williams¹⁸ mentioned three basic types of food allergens as being responsible for mild to severe oedema of the laryngeal structures:

Fixed food allergy will still produce symptoms on each ingestion, regardless of the time when it was eliminated from the diet or the amount ingested.

Cyclic food allergy, which can be controlled by elimination or rotation of a food in the diet, while continuative usage is responsible for sensitization and symptoms.

Thermal food allergy, which is triggered by the exposure to a low temperature "critical for the patient".

Particles of dietary antigens may adhere to the mucosa of the arytenoid region and consequently may cause direct oedema in this region¹².

In our study, we have reported milk intolerance in 10 patients (13.2%).

On the other hand, inhaled antigens may enter the post-nasal drip and may reach the arytenoid region by mucociliary transport¹².

Laryngeal oedema may be the only symptom of hypersensitivity to salicylic acid or other substances which affect the biosynthesis of prostaglandins, such as other analgesics or certain colour additives and preservatives in food¹⁹. We have found allergy to drugs in 9 cases (11.8%): 3 were allergic to salicylic acid and FANS, 6 were allergic to penicillin and derivatives.

In the event of allergic rhinitis, the hypersecretion of the nasal glands is responsible for a postnasal drainage onto oropharyngeal and laryngeal tissue: the consequences are throat clearing, irritating cough, and dysphonia²⁰. According to our study, allergic rhinitis was present in 43 patients (56.6%).

Another mechanism hypothesised to explain cases of dysphonia secondary to allergic rhinitis is based on the presence of rhino-laryngeal reflexes: the presence of va-

somotor and secretomotor fibres of sympathetic and parasympathetic origin have been demonstrated in the mucosa and in the *musculus vocalis*, particularly in the posterior third of the vocal cords^{21,22}.

Specific receptors in the laryngeal mucosa are sensitive to negative pressure in the nasal cavity and in the rhinopharynx²³. A negative nasal pressure due to allergic rhinitis is responsible for a reflex increase of the muscular activity of the posterior crico-arytenoid, as recorded by electromyography²⁴.

Another correlation between allergic rhinitis and vocal disorders may be mediated by the diminished hearing. In fact, it has been estimated that serous otitis occurs in about 66% of children affected by allergic rhinitis¹. The consequent conductive hearing loss may induce vocal abuse.

Gastro-oesophageal reflux is not a rare finding in laryngeal disorders²⁵. Professional voice users, whose performances need an increase of abdominal pressure are at high risk of gastro-oesophageal reflux disease (GERD). We have found gastro-oesophageal reflux in 15 patients (19.7%).

Both allergic reactions and autonomic imbalance may result in the respiratory mucosa becoming hyper-reactive to unspecific irritants²⁶.

The methacholine challenge may show a non-specific bronchial reactivity in professional voice users presenting with voice complaints and responding to bronchodilators and to allergy-directed therapy. In other words, in these patients, the hyperventilation associated with performing is responsible for an exercise-induced asthma-like condition, related to voice dysfunction: resolution of the vocal complaints has been recorded in conjunction with a decrease in methacholine reactivity²⁷.

A history of seasonal/perennial allergy symptoms was reported in 37% of 150 patients seen by Altman et al.²⁸.

The total prevalence of allergic rhinitis was 87% in the group of singers studied by Hamdan et al.²⁰. Both figures exceeded the average prevalence of 25% observed in the general population²⁹.

In our study, muscle tension dysphonia and nodules were present, respectively, in 32.9 and in 42.1% of the subjects. As 76.3% of patients presenting with dysphonia were also allergic, it may be concluded that this result is higher than the well-known average prevalence of 25%.

With regard to the association between female sex and presence of allergy in patients suffering from dysphonia, the application of Pearson's chi square revealed a significant association between female sex and presence of allergy in dysphonic patients (Pearson's chi square = 7.89, $P = 0.005$).

Furthermore, sex was considered as a "risk factor" and was associated with each disease detected. A statistically significant association had been revealed between female sex and presence of allergy (OR 5.51; CI: 1.55-19.63). In the same subjects being female was shown to be a "pro-

protective factor" against gastro-oesophageal reflux (OR. 0.12; CI: 0.03-0.46) (Table IV).

This same statistical analysis was shown to be not significant for the other above-mentioned diseases.

Conclusions

According to our study, allergy testing should be performed routinely on female professional voice users. Singers, actors, teachers, physicians, politicians, secretaries, call-centre operators, football quarterbacks are the best known people whose voice troubles impair job performances³⁰. Dust and mold found in curtains and trappings, chemical fumes, smoke, animal exposure, costumes, perfumes, cosmetics are only a few examples of the several common and less common antigens, that can be responsible for allergic problems.

Mild respiratory disorders, that may not be particularly relevant in the general population, must be taken into serious consideration in female professional voice users, who may primarily complain of vocal dysfunction rather than upper and lower respiratory diseases²⁰.

Twenty-four-hour intraluminal oesophageal pH monitoring should be included in the diagnostic examinations, particularly in the case of males.

If chronic vocal disorders are the reason for therapy, the possibility of allergy as the cause should be carefully evaluated³¹ and skin prick testing is mandatory. We agree with Pedersen et al.⁴ that the doctors should examine any other diagnosis besides "dysphonia" and "dig down to" any of the medical reasons of the "non-organic disorders". Therefore, we can conclude with the recommendation made by Moore³² to remember that "the remediation of voice disorders encompasses more than voice assessment and voice exercises".

References

- Baker BM, Baker CD, Thanh Le HA. *Vocal quality, articulation and audiological characteristics of children and young adults with diagnosed allergies*. Ann Otol Rhinol Laryngol 1982;91:277-80.
- Senturia BH, Wilson FB. *Otorhinolaryngologic findings in children with voice deviation*. Ann Otol Rhinol Laryngol 1948;77:1027-41.
- Haapanen ML. *Provoked laryngeal dysfunction*. Folia Phoniatr 1990;42:157-69.
- Pedersen M, Beranova A, Moller S. *Dysphonia: medical treatment and a medical voice hygiene advice approach. A prospective randomised pilot study*. Eur Arch Otorhinolaryngol 2004;261:312-5.
- Hirano M. *Surgical anatomy and physiology of the voice*. In: Gould WJ, Sataloff RT, Spiegel JR. editors. *Voice surgery*. Chicago, IL: Mosby-Yearbook; 1993. p. 135-58.
- Cohn JR, Spiegel JR, Sataloff RT. *Vocal disorders and the professional voice user: the allergist's role*. Ann Allergy Asthma Immunol 1995;74:363-75.
- Niedzielska G. *Acoustic estimation of voice when incorrect resonance function of the nose takes place*. Int J Pediatr Otorhinolaryngol 2005;69:1065-9.
- Roth DF, Ferguson BJ. *Vocal allergy: recent advances in understanding the role of allergy in dysphonia*. Curr Opin Otolaryngol Head Neck Surg 2010;18:176-81.
- Yamashita T, Yamaguchi M, Ishitani Y, et al. *One case of histopathologically demonstrated laryngeal allergy: provocation test with sensitization antigens*. Larynx Jpn 1989;1:102-4.
- Grahne B. *The mast cell count in the subepithelial tissue of the larynx, trachea and bronchi of human embryos*. Acta Path Microbiol Scand 1995;46(suppl. 131):1-64.
- Buczylko K, Reezen H. *Allergic laryngitis*. Pol Merkur Lek 1999;7:95-8.
- Takeda N, Yamaguchi M, Yamashita T, et al. *Laryngoscopic findings in cases of laryngeal allergy*. In: Mogi G, Veldman JE, Kawauchi H, editors. *Immunobiology in Otorhinolaryngology - Progress of a Decade*. Amsterdam/New York: Kugler Publications; 1994.
- Halsted TH. *Angioneurotic edema involving the upper respiratory tract*. Trans Amer Laryng Assn 1905;27:7.
- Hansel FK. *Clinical allergy*. St Louis: C.V. Mosby Co.; 1953.
- Moses P. *The voice of the neurosis*. New York: Grune & Stratton Inc; 1954.
- Paparella M. *Unusual foreign body of trachea and intrinsic bee sting of larynx*. J Laryngol 1964;78:89-92.
- Wolf IJ. *Allergic factors in the etiology of spasmodic croup and laryngo-tracheitis*. Amer Allergy 1966;24:79-82.
- Willams RI. *Allergic laryngitis*. Ann Otol 1972; 81:558-65.
- Hillerdal G, Lindholm H. *Laryngeal edema as the only symptom of hypersensitivity to salicylic acid and other substances*. J Laryngol Otol 1984; 98:547-8.
- Hamdan A-L, Sibai A, Youssef M, et al. *The use of a screening questionnaire to determine the incidence of allergic rhinitis in singers with dysphonia*. Arch Otolaryngol Head Neck Surg 2006;132:547-9.
- Konig WF, von Leden H. *The peripheral nervous system of the human larynx*. Archs Otolaryngol (Parts I, II and III) 1961;73:114; 74:153-163; 494-500.
- Wyke BD, Kirschner JA. *Neurology of the larynx*. London: Heinemann, Scientific Foundations of Otolaryngology; 1976. p. 546-74.
- Sant'Ambrogio G, Mathew OP, Fisher ST, et al. *Laryngeal receptors responding to transmural pressure, airflow and local muscle activity*. Respir Physiol 1983;54:317-30.
- van Lunteren E, van de Fraaff WB, Parker DM, et al. *Nasal and laryngeal reflex responses to negative upper airway pressure*. J Appl Physiol 1984;56:746-52.
- Koufman JA, Wiener GJ, Wu WC, et al. *Reflux laryngitis and its sequelae: the diagnostic role of ambulatory 24-hour pH monitoring*. J Voice 1988;2:78-89.
- Mygind N. *Nasal allergy*. Oxford: Blackwell; 1978.
- Cohn JR, Sataloff RT, Branton C. *Response of asthma-related voice dysfunction to allergen immunotherapy: a case report of confirmation by methacholine challenge*. J Voice 2001;15:558-60.

- ²⁸ Altman KW, Atkinson C, Lazarus C. *Current and emerging concepts in muscle tension dysphonia: a 30 months review*. J Voice 2005;19:261-7.
- ²⁹ Bousquet J, van Cauwenberg P, Khaltaev N. *Allergic rhinitis and its impact on asthma*. J Allergy Clin Immunol 2001;108 (Suppl.):S317-34.
- ³⁰ Jackson-Menaldi CA, Dzul AI, Holland RW. *Hidden respiratory allergies in voice users: treatment strategies*. Logoped Phoniatr Vocol 2002;27:74-9.
- ³¹ Randhawa PS, Mansuri S, Rubin JS. *Is dysphonia due to allergic laryngitis being misdiagnosed as laryngopharyngeal reflux?* Logoped Phoniatr Vocol 2010;35:1-5.
- ³² Moore GP. *Organic voice disorders*. Englewood Cliffs: Prentice-Hall; 1971.

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