

Polyvinyl Chloride Film Thermal Decomposition Products as an Occupational Illness

2. Clinical Studies

Stuart M. Brooks, M.D. and Robert Vandervort

In 1973, Sokol et al reported three cases of workers employed as meat wrappers who developed respiratory symptoms when exposed to fumes of polyvinyl chloride (PVC) film cut with a hot wire.¹ The patients were middle-aged women who smoked cigarettes and demonstrated reversible airway obstruction on pulmonary function testing. The patients were not studied at work, but reported to a hospital where examinations and laboratory studies were performed. In an epidemiologic study conducted in 152 supermarkets in Houston, Tex., approximately 10% of the meat wrappers studied reported multiple respiratory symptoms at work which included wheezing, shortness of breath, and chest pain or tightness.² A significantly greater prevalence of symptoms suggesting eye, nose and throat irritation was also found. Andrasch et al conducted a questionnaire survey of 165 meat wrappers in the Portland, Ore. metropolitan area.³ Fifty-seven percent of the symptomatic workers reported respiratory symptoms and 30% reported symptoms suggestive of nose and throat irritation. Several workers reported the occurrence of acute asthmatic attacks while at work. Bronchial inhalation provocation studies with emissions from hot-wire cutting of PVC films conducted on 11 selected meat wrappers demonstrated rhinorrhea in seven wrappers, cough, tightness of the chest, and sore throat in five, dyspnea, exhaustion and wheezing in four, and throat soreness in two subjects. These studies were conducted in a laboratory away from work. Nine of 13 patients who were then challenged with emissions from heating price label material developed immediate acute asthmatic reactions. Four of these subjects also experienced a delayed asthmatic reaction which occurred six to eight hours after exposure. The authors concluded that the emissions from thermally activating price labels were the principal cause of "meat wrappers asthma," but that the entire spectrum of this disease had to be interpreted as a complex

response from exposure to both emissions from hot-wire cutting of PVC film and from thermal activation of price labels. Other investigations of respiratory illness in meat wrappers have also been reported.³⁻⁶

The Bureau of Occupational Safety & Health received complaints associated with exposure to air contaminants generated by the hot wire cutting of PVC meat packaging film as early as the summer of 1969. Beginning in 1972, The National Institute for Occupational Safety & Health conducted clinical studies of meat wrappers in response to requests for Health Hazard Evaluations in supermarket meat departments. The present report contains the results of these clinical studies. Investigation of many of these cases was in collaboration with the Department of Environmental Health, University of Cincinnati College of Medicine.

Materials and Method

Twenty-four meat wrappers, eight meat cutters and 20 control subjects (office personnel and store clerks) make up the population studied. Data concerning age, sex and smoking history of the subjects are shown in Table 1. While meat wrappers were commonly women, meat cutters were usually men. The three groups were of similar age, but there was a greater number of meat wrappers who were cigarette smokers. The mean duration of wrapping in the meat wrappers was 12.5 years (range 1 to 26 years).

Investigations were performed at or near the workplace in each case. The meat cutters worked in the same general area as the meat wrappers. Each subject was administered a modified respiratory questionnaire which included questions on past medical history, cigarette smoking, previous occupational exposures, current respiratory status and adverse effects allegedly arising from work.

Pulmonary function testing was performed on each of the 53 workers at the beginning and end of the work shift. Thirty-seven subjects were tested using a waterless, high fidelity, precalibrated spirometer equipped with an air temperature probe (Ohio Medical

From the Department of Environmental Health, University of Cincinnati, Cincinnati, Ohio 45267 (Dr. Brooks) and DB Associates, Inc., Salt Lake City (Mr. Vandervort, formerly Industrial Hygienist, NIOSH).

Table 1. — Study Population.					
	No.	Mean Age (years)	Sex		% Smokers
			Male	Female	
Meat Wrappers	24	41	12	12	50
Meat Cutters	8	40	6	2	25
Controls	20	40	14	6	20

Products, Madison, Wis.). In 15 subjects, tests were performed using a precalibrated wedge-bellows spirometer (Vitalograph Medical Instrumentation, Kansas City, Mo.). Precalibration was made using a calibration syringe prior to field study. Forced vital capacity (FVC) and forced expiratory volume at one second (FEV₁) were measured in all subjects. Maximum expiratory flow rates at 50 and 25% of the vital capacity (\dot{V}_{50} and \dot{V}_{25}) were measured in 37 subjects (utilizing the waterless high fidelity spirometer). Maximum mid-expiratory flows (MMF) were determined for 15 subjects using the wedge-bellows spirometer. Predicted normal values were those reported by Morris & Associates.⁷ Pre and post-shift complete blood and total eosinophil counts were performed on 15 subjects (seven meat wrappers and eight meat cutters).

Results

(a) Symptomatology Away from Work. — Respiratory and nasal symptoms occurring away from work were common in both meat wrappers and cutters (see Table 2). Two of the eight meat cutters had the diagnosis of bronchial asthma and were being treated by their physicians. One other meat cutter had symptoms suggestive of allergic rhinitis. Thus, three of eight meat cutters had chronic symptoms which could have been related to underlying bronchial asthma or allergic rhinitis.

Approximately one-third of the meat wrappers had complaints of chronic cough and/or sputum or dyspnea on exertion. A physician's diagnosis of asthma or allergic rhinitis was noted in 17% (4 of 24) of the meat wrappers.

(b) Symptomatology at Work. — The symptoms occurring at work as reported by the subjects are shown in Table 3. The mean duration of meat wrapping performed during the day of the respective study was 5.8 hours (range 0.5 to 8.0 hours).

Sixty-seven percent (16 of 24) of the meat wrappers had at least one symptom which they attributed to work. The most common complaints were related to throat, eye and nasal symptoms. These included dry or sore throat; burning, itchy or tearing eyes; and stuffy or runny nose. The frequency of throat, eye and nasal symptoms in the 16 symptomatic meat wrappers were 62, 50 and 19%, respectively. Symptoms of cough, chest tightness, wheezing,

Table 2. — Symptoms Away From Work.			
Symptom	% Reporting Symptoms		
	Meat Wrappers (n = 24)	Meat Cutters (n = 8)	Controls (n = 20)
Cough and/or sputum	37	75	10
Dyspnea on exertion	29	50	10
Wheezing	12	37	0
Frequent chest illnesses	4	12	5
Asthma/Allergy history	17	25	5
Nasal symptoms	14	62	0

shortness of breath, and chest pain occurred in 31, 17, 12, 50 and 25% of the symptomatic meat wrappers, respectively. Twenty-five percent (4 of 14) of the symptomatic meat wrappers had a physician's diagnosis of bronchial asthma or allergic rhinitis. Forty-five percent (7 of 16) of the symptomatic meat wrappers were cigarette smokers. These individuals represent 58% (7 of 12) of all smoking meat wrappers. Forty-four percent (7 of 16) of the symptomatic meat wrappers had chronic complaints of cough and/or sputum, and 37% (6 of 16) reported chronic dyspnea on exertion.

The meat cutters did report a high frequency of symptoms at work. The group of meat cutters is small and of those reporting symptoms, three were those individuals who were previously identified as having either bronchial asthma or allergic rhinitis, or both.

During the performance of these investigations, workers were carefully questioned regarding the probable cause of their work-related symptoms. In general, all workers expressed the opinion that emissions from the hot wire cutting of PVC film were responsible. A few workers felt that the refrigerated working environment or a pre-existing medical condition may be contributing to the symptoms experienced at work. At the same time of the respective field visits, none of the workers were questioned specifically about the emissions from the thermal activation of price labels. Following the presentation of Andrash et al,³ workers at three supermarkets studied were contacted by phone. Thirteen of the original 15 workers studied were questioned regarding emissions from the label machinery. All workers denied ever noticing any objectionable emissions. A few mentioned that a label would occasionally be scorched by the heating unit, but that their work stations were sufficiently far away from the labeling machinery that the occasional emissions (light smoke) did not present a noticeable problem.

Table 3. — Symptoms at Work.				
Symptom	Meat Wrappers		Meat Cutters (n = 8)	Controls (n = 20)
	Total (n = 24)	Symptomatic (n = 16)		
Throat	42	62	50	5
Eye	13	50	37	15
Nasal	12	19	62	0
Cough	21	31	37	0
Chest tightness	29	37	50	0
Wheezing	8	12	25	0
Shortness of breath	37	50	50	0
Chest pain	17	25	37	0
Smokers	50	44	25	20

Table 4. — Pulmonary Function Test Results, Pre and Postshift (Mean \pm 1 Standard Deviation).

Tests	Meat Wrappers				Meat Cutters				Controls	
	Total (n = 24)		Symptomatic (n = 16)		Total (n = 8)		Asymptomatic (n = 8)		(n = 20)	
	Pre	Post*	Pre	Post*	Pre	Post*	Pre	Post*	Pre	Post*
FVC, L	4.18 \pm 1.11	4.12 \pm 1.10	4.10 \pm 1.0	4.06 \pm 1.0	4.36 \pm 1.11	4.31 \pm 0.97	4.11 \pm 1.19	4.08 \pm 1.16	4.11 \pm 1.19	4.08 \pm 1.16
% of Pred.	99 \pm 18	99 \pm 18	99 \pm 14	99 \pm 14	102 \pm 13	102 \pm 13	105 \pm 17	105 \pm 17	105 \pm 17	105 \pm 17
FEV ₁ , L	3.29 \pm 0.88	3.25 \pm 0.87	3.34 \pm 0.86	3.28 \pm 0.87	3.48 \pm 0.84	3.40 \pm 0.83	3.34 \pm 1.06	3.29 \pm 1.04	3.34 \pm 1.06	3.29 \pm 1.04
% of Pred.	101 \pm 20	101 \pm 20	103 \pm 18	103 \pm 18	105 \pm 20	105 \pm 20	110 \pm 17	110 \pm 17	110 \pm 17	110 \pm 17
MMF, L/sec	3.61 \pm 0.98	3.78 \pm 0.86 (n = 7)	3.78 \pm 0.95 (n = 6)	3.96 \pm 0.79 (n = 6)	3.16 \pm 0.94	3.10 \pm 1.01	—	—	—	—
\dot{V}_{50} , L/sec	3.66 \pm 1.14 (n = 17)	3.65 \pm 1.25 (n = 17)	3.95 \pm 1.13 (n = 10)	3.85 \pm 1.33 (n = 10)	—	—	4.41 \pm 1.76	4.34 \pm 1.68	4.41 \pm 1.76	4.34 \pm 1.68
\dot{V}_{25} , L/sec	1.17 \pm 0.64 (n = 17)	1.11 \pm 0.58 (n = 17)	1.31 \pm 0.72 (n = 10)	1.23 \pm 0.68 (n = 10)	—	—	1.53 \pm 0.76	1.48 \pm 0.90	1.53 \pm 0.76	1.48 \pm 0.90

*Postshift test results were not significantly different from preshift values ($p > 0.05$)

(c) **Pulmonary Function Tests.** — Results of pulmonary function testing are shown in Table 4. The mean preshift FVC (forced vital capacity) and FEV₁ (forced expiratory volume at one second) were within normal limits for all groups. No significant differences in pre and postshift pulmonary function test results were noted for any group.

(d) **Blood Analyses.** — The results of tests performed on blood drawn from 15 subjects (seven meat wrappers and eight meat cutters) are presented in Table 5.

No significant pre to postshift increases in mean white blood cell or total eosinophil counts were observed.

(e) **Symptomatic Meat Wrapper.** — In the course of the health hazard evaluation investigations, a particularly interesting case of an affected meat wrapper was encountered. Prior to employment as a meat wrapper, this person had no remarkable health problems and was a nonsmoker. Information regarding this particular case will be presented because of the nature of the documented medical data available.

The subject was a 37 year old woman who had worked as a meat wrapper for a total of 16 years. She described the development of a nonproductive cough and exertional dyspnea occurring two years prior to our contact with her. There was no previous history of wheezing, allergic rhinitis, serious chest illness, or family history of asthma or hay fever.

The subject stated that, beginning in November 1973 (five months prior to our visit), following a change to a new wrapping film, she began noticing shortness of breath, tightness of the chest, chest pain, cough, skin rash and swelling of the eyes. She related having experienced a similar problem five years before. According to the subject, the chest symptoms were not present during the first 1 to 1.5 hours of wrapping, but appeared later in the work day. The respiratory symptoms reportedly became worse as the work week progressed and also occurred at home. During the weekend the symptoms were reported to disappear but would reappear and progressively worsen during the work week. She did consult a physician who treated her with corticosteroids. This relieved the facial swelling, but the shortness of breath persisted. Her respiratory symptoms reportedly disappeared following the discontinuation of the use of the new meat wrapping film.

Three weeks prior to our visit to her place of employment, the new wrap was again introduced and her symptoms returned. She described the new PVC wrap as being a "heavy wrap" as compared to the "light wrap" utilized previously. Several days before our visit, the subject sought medical treatment and was referred to an allergist for complete workup. Skin tests were found to be

negative for animal dander, feathers, cottonseed, pollen, mold, dust, tree, grass, ragweeds, and housedust. The physician noted wheezing which cleared during the period the patient was off work. Two days prior to our visit, the subject performed pulmonary function tests at a private hospital laboratory. At the time of this testing the subject was symptomatic and was still being treated with medication by her physician.

The study team saw the subject on her first day back at work. The subject stated that her respiratory symptoms had recently completely cleared. The subject was observed while wrapping meat for six hours. During the shift she became symptomatic, complaining of dry sore throat, progressively worse cough, a feeling of tightness in the chest and shortness of breath. Physical examinations performed at intervals through the shift were entirely negative and included the absence of wheezing and rhonchi. There was no significant change in white blood cell count or total eosinophil count over the observed shift. Pulmonary function test results from studies performed at her place of employment and from studies performed two days before by the private hospital laboratory are shown in Table 6. No significant response in pulmonary function tests to three inhalations of isoproterenol given at the end of the work shift was observed. The preshift MMF was 71% of predicted but increased to 86% of predicted by the end of the day indicating a greater than 20% improvement (this was without isoproterenol inhalation).

Tests taken two days earlier, when the subject was still symptomatic and under treatment, show reduced MMF, and abnormal closing capacity/total lung capacity ratio. In addition, there was a small improvement in FEV₁ and significant improvement in MMF following administration of bronchodilators.

Discussion

The present evaluation of available data demonstrates that no acute changes in pulmonary function testing occurred in 24 meat wrappers exposed to air contaminants in the meat wrapping environment while at work. Additionally, in a group of seven meat

Table 5. — Results of Blood Analyses.

	White Blood Cell Count		Total Eosinophil Count	
	Preshift	Postshift	Preshift	Postshift
Meat Wrappers	8081 \pm 1730	7944 \pm 2077	187 \pm 115	212 \pm 137
Meat Cutters	7268 \pm 2289	7953 \pm 1853	230 \pm 101	134 \pm 89

Table 6. — Pulmonary Function Test Results of a Symptomatic Meat Wrapper.

Tests	Private Lab Test Results (2 days before work test)	Pulmonary Function Testing at Work	
		Pre-shift	Postshift
FVC (% predicted)	95	91	91
FEV ₁ (% predicted)	85	91	94
MMF (% predicted)	57	71	86
% Improvement Following			
Bronchodilator			
FEV ₁	93		4.6
MMF	43		0
Other Parameters (% Pred.)			
Peak Expiratory			
Flow Rate	93		
\dot{V}_{50}	59		
CC/TLC %	131		
CC%	128		
RV%	96		
TLC%	97		
CC = Closing Capacity			
RV = Residual Volume			
TLC = Total Lung Capacity			

wrappers and eight meat cutters, no significant increase in post-shift white blood cell and total eosinophil count occurred. The meat cutters were noted, in fact, to have a fall in total eosinophil count.

Approximately one-third of the 24 meat wrappers studied had chronic complaints of cough, sputum and dyspnea on exertion. These data are consistent with those of Falk and Portnoy and suggest that chronic exposure to air contaminants in the meat wrapping environment may lead to chronic respiratory complaints.²

In contrast to the report of Andrasch et al, no apparent cause-effect relationship can be made in this study between emissions from price label activation and respiratory complaints.³ Thirteen of the 15 most recently studied workers denied noticeable effects from price label emissions.

No relationship was observed between cigarette smoking in meat wrappers and the likelihood of developing respiratory symptoms. Twice as many meat wrappers as controls were cigarette smokers (50 vs. 20%). Falk and Portnoy, in a larger study, concluded that meat wrappers who smoke were at greater risk of developing respiratory symptoms than nonsmoking meat wrappers.²

Several of the workers in this study did relate symptoms to the use of a specific meat wrap. Due to the small numbers of workers available for study, it was not possible to statistically confirm this observation. Falk and Portnoy could not relate a greater prevalence of respiratory complaints to a specific meat wrap.²

The designation "meat wrappers asthma" is a minomer. Classic allergic bronchial asthma is characterized by intermittent wheezing, eosinophilia, and reduced FEV₁ and MMF.⁸ Symptomatic meat wrappers in the present investigations did not demonstrate any of these findings. Those workers who had underlying bronchial asthma, however, seemed more likely to complain of wheezing and cough at work. This is not unexpected since individuals with bronchial asthma have hyperreactive airways that respond by bronchoconstricting following exposure to many nonspecific irritants.⁸⁻⁹ Vagally mediated subepithelial cough-reflex receptors, as well as other mechanisms, may be important in this regard.¹⁰⁻¹² Emissions from hot-wire cutting of

PVC film and from thermal activation of price labels contain substances that are known for their irritative effects.⁶

Inhalation to PVC fumes may, in itself, induce a state of bronchial hyperreactivity not on an allergic basis. Boushey and associates studied the effects of PVC fumes on pulmonary function in 10 meat wrappers who had respiratory symptoms attributed to their work.¹³ Testing of airway reactivity to histamine aerosol was performed in each subject. This study suggested that increased bronchial reactivity to histamine aerosol characterized patients who developed severe respiratory symptoms on exposure to PVC fumes. Inhalation of PVC fumes in a laboratory for periods up to three hours did not alter pulmonary function in the subjects; however, such an inhalation, in itself, induced a state of bronchial hyperreactivity as defined by a greater increase in airway resistance to histamine inhalation after these subjects were exposed to PVC fumes. The lack of change in pulmonary function testing following inhalation of PVC fumes in the study of Boushey et al is consistent with the findings in the present investigation. Prolonged and/or chronic exposure to PVC fumes could perhaps result in greater airway hyperreactivity and thus result in physiologic and clinical changes at work. There were no physiologic changes, however, noted in the present investigation.

The report of Andrasch et al is difficult to evaluate, since the challenge experiments with price label emission were not comparable to actual working conditions and, in general, constituted exaggerated exposure.³ Although bronchospasm and reduced FEV₁ were demonstrated in selected patients, it is not clear from the report whether individuals had pre-existing bronchial asthma. In addition, it is not apparent whether the effects noted were the result of actual sensitization, consequence of direct irritation, or due to increased airway reactivity.

The detailed pulmonary function studies performed on our most symptomatic meat wrapper suggest possible involvement of the small airways of the lung. These are the airways 2 mm and less in diameter.¹⁴ Normal FEV₁ and FVC, but reduced MMF and \dot{V}_{50} , and elevated CC% and CC/TLC% (demonstrated two days prior to our study) are findings reported to indicate small airways disease.¹⁵⁻¹⁷ This mechanism has been proposed by others.⁴ Patients with bronchial asthma may show evidence of persistent

abnormalities of small airways even during a period of remission.¹⁸⁻¹⁹ Complaints of chest tightness and dyspnea could be manifestations of small airways involvement. Interestingly, asymptomatic cigarette smokers have also been reported to show normal spirometric testing but have pathologic and physiologic evidence of small airways disease.¹⁴⁻²⁰ Macklem has postulated that chronic obstructive pulmonary disease (eg, emphysema and/or chronic bronchitis) in its beginning stage is manifested by involvement of the small airways.¹⁴ At this stage in time, the usual spirometric tests such as FEV₁ or FVC are normal. It is only after many years of smoking that individuals become symptomatic and develop abnormalities on routine pulmonary function testing (eg, FEV₁ and FVC). This theoretical mechanism may be pertinent if air contaminants in the meat wrapping environment are capable of causing small airways disease. Absorption of irritative substances on small aerosol particles contained in the emissions from film hot-wire cutting and label activation may allow deeper penetration of the irritants into the airways. Fifteen to 20 years and more of exposure to contaminants in the meat wrapping environment may be necessary before changes occur in the pulmonary function tests. It is possible that the pulmonary function testing equipment used in the present study was not of sufficient sensitivity to detect changes in small airways. It must be noted, however, that in the portion of the workers studied, no significant changes in pre and postshift MMF, \dot{V}_{50} and \dot{V}_{25} were observed when these tests were performed. Changes in these tests have been reported as indicative of small airways disease.¹⁵⁻¹⁶⁻¹⁷

Whether cigarette smoking and exposure to the meat wrapping environment has an additive effect on small airways is not known. Persons with diagnosed bronchial asthma and clinically significant chronic obstructive pulmonary disease should avoid exposure to poorly controlled meat wrapping work environments since it may aggravate their disease. The long-term pulmonary effects of inhalation of PVC meat wrapping film is presently not known and requires further study. Until definitive information is available, every effort should be made to reduce contaminant concentrations in the meat wrapping environment.

Summary and Conclusions

Exposure to air contaminants emitted into the meat wrapping environment may produce acute health effects in some individuals. The effects relate primarily to eye, nose and throat irritation. Individuals with bronchial asthma and other types of chronic obstructive respiratory disease may develop bronchospasm as the result of exposure to the irritants emitted. It cannot be determined from these studies whether actual allergic sensitization and resultant bronchial asthma occurs from exposure to these contaminants. If actual allergic sensitization does occur, it does not appear to be common. There is a possibility that changes may occur in the small airways of the lung as the result of exposure to PVC contaminants. The significance of these changes, if real, cannot be determined from the available data. The high reported prevalence of chronic respiratory symptoms in the meat wrappers studied suggests possible long-term effects from exposure to the air contaminants in the meat wrapping environment. The significance of chronic symptoms cannot be determined since, in general, pulmonary function test results for individuals studied were within normal limits. It is possible that the duration of ex-

posure is not yet sufficient to result in spirometric changes. To completely answer all questions regarding possible effects from exposure to these air contaminants would require careful study of large numbers of exposed individuals over time using sophisticated pulmonary function testing equipment. Persons with bronchial asthma and clinically significant chronic obstructive pulmonary disease should avoid exposure to poorly controlled meat wrapping work environments. Until definitive information is available, every effort should be made to reduce contaminant concentrations in the meat wrapping environment.

Much of this work was accomplished in a collaborative study by The Clinical Studies Division, Department of Environmental Health, University of Cincinnati College of Medicine and the Hazard Evaluation Services Branch, National Institute for Occupational Safety and Health, Center for Disease Control, U.S. Department of HEW. The helpful assistance in clinical evaluation of Robert Ligo, M.D., Robert Rostand, M.D., and Philip Polakoff, M.D., is graciously acknowledged. Pulmonary function test results were kindly supplied by Edward Chester, M.D., Case Western Reserve Medical College, Cleveland, Ohio.

References

1. Sokol WN, Aelony Y, Beall GN: Meat wrapper's asthma a new syndrome. *JAMA* 226(6):639, 1973.
2. Falk H, Portnoy B: Respiratory illness in meat wrappers. *JAMA* 235:915, 1976.
3. Andrasch RH, Koster F, Lawson WH et al: Meat wrappers' asthma — An appraisal of a new occupational syndrome. *J Allergy & Clin Immunol* 55:130, 1975.
4. Polakoff PL, Lapp NL, Reger R: Polyvinyl chloride pyrolysis products a potential cause for respiratory impairment. *Arch Environ Hlth* 30:269, 1975.
5. Johnson CJ and Anderson JW: Meat wrappers asthma: A case study. *JOM* 18:102, 1976.
6. Vandervort R and Brooks SM: Health Hazard Evaluation Determination report No. 74-24, 92, 95. USDE/EW, NIOSH, Oct. 1975.
7. Morris JF, Koski A, Johnson LC: Spirometric standards for healthy non-smoking adults. *Amer Rev Resp Dis* 103:37, 1971.
8. Terr: Bronchial Asthma, in Text Book of Pulmonary Diseases, edited by Gerald L. Baum, M.D., Tuttle, Brown and Co., Boston, p. 421, 1974.
9. Mathison DA, Stevenson SD, Tan EM, Vaughan JH: Clinical profiles of bronchial asthma. *JAMA* 224:1134, 1973.
10. Simmons BG, Jacob FM, Nadel JA: Role of the autonomic nervous system and the cough reflex in the responsiveness of airways in patients with obstructive airway disease. *J Clin Invest* 46:1812, 1967.
11. Nadel JA: Mechanisms of airway response to inhaled substances. *Arch Environ Hlth* 16:171, 1968.
12. Szentivanyi A: The beta adrenergic theory of atopic abnormality in bronchial asthma. *J Allergy* 42:203, 1968.
13. Boushey HA, Empey DW and Laitinen LA: Meat wrapper's asthma: Effect of fumes of polyvinyl chloride on airway function Page 29 — *Physiologist* 18:148, 1975.
14. Macklem P: Obstruction in small airways — A challenge to medicine. *Amer J Med* 52:721, 1972.
15. McFadden ER Jr, Linden DA: A reduction in maximal mid-expiratory flow rate. A spirographic manifestation of small airway disease. *Amer J Med* 52:725, 1972.
16. Gelb AF, Zamel N: Simplified diagnosis of small airway obstruction. *New Engl J Med* 288:395, 1973.
17. McCarthy DS, Spence R, Greene R, Melec-Emili J: Measurement of "closing volume" as a simplified and sensitive test for early detection of small airways disease. *Amer J Med* 52:747, 1972.
18. McCarthy DS, Melec-Emili J: Closing volume in asymptomatic asthma. *Amer Rev Respir Dis* 107:559, 1973.
19. Anthonisen NR, Bass H, Oriol A, Place REG, Bates DV: Regional lung function in patients with bronchial asthma. *Clin Sci* 35:495, 1968.
20. Ingram LH Jr, O'Cain CF: Frequency Dependence of Compliance in Apparently Healthy Smokers Versus Nonsmokers, Lung and Airway Mechanics in Normal Men and in Chronic Lung Diseases. *Entretiens de Physio-Pathologic Respiratoire, Nancy 8e Series (Peslin R. Ed.)*, Masson and Cie, Paris, 1971.