MEDICAL GRAND ROUNDS

Parkland Memorial Hospital

April 2, 1964

CHRONIC BRONCHITIS

I. Definition - Chronic bronchitis is a persistent or recurring cough with sputum production; and as such is a broad descriptive term that needs specific elucidation in each patient situation.

II. Pathological Characteristics
- A. Tissue
- B. Sputum

III. Etiological Considerations
- A. Non-specific physio-chemical irritants, inhaled
  - 1. Tobacco smoke inhalation
  - 2. Local and general air pollutants
- B. Infectious agents
  - 1. Bacterial
    - a. D. pneumoniae
    - b. H. influenza
    - c. Gram negative rods
    - d. Coag. pos. Staph. aureus in C.F.
    - e. Strep. pyogenes
  - 2. Viral and related agents
    - a. Influenza viruses
    - b. Adenovirus (3, 4, 7 & 14)
    - c. Eaton agent (P.A.T.)
    - d. Para influenza myxoviruses (1-4)
    - e. Echo viruses (10, 11, 20, 28) may only precipitate exacerbations
- C. Specific inciting agents
  - 1. Extrinsic antigens
  - 2. Intrinsic antigens
    - a. Autoimmune reactions
    - b. Bacterial antigens
- D. Non-specific irritants endogenous
  - 1. Bacteria or bacterial products
  - 2. Retained products of tissue injury
  - 3. Vascular congestion - L.V.F.
- E. Constitutional or host factors often set the stage

IV. Clinical Features
- A. Radiological
- B. Physiological
  - 1. Types of obstruction
  - 2. Bronchitis vs. emphysema
- C. Complications
  - 1. Respiratory insufficiency
  - 2. Cor pulmonale

V. Treatment

CASE [redacted]

A 28 year old white female mental defective with 18 PMH admissions, had 9 admissions from 1953 - 1960 for meningitis, tonsillitis, T & A, 4 deliveries, appendectomy and abortion.

There were two admissions for a collagen disorder never conclusively classified but characterized by anemia, rheumatoid arthritis, fever, a pruritic, erythematous, urticarial, skin rash, lymphadenopathy, and hypergammaglobulinemia.

She was known to be a heavy smoker having smoked and inhaled one or more packages of cigarettes per day for 14 years.

Her 12th - 16th admissions revealed evidence of acute and chronic bronchopulmonary infection severe, due to pneumococci. During this time her skin eruption was under treatment with steroids. Two liver biopsies, 3 kidney biopsies, skin and lymphnode biopsies failed to yield a specific etiologic diagnosis. She had a persistent, progressive, productive cough with increasing shortness of breath.

Her 17th admission (two months before her death) was for extensive pulmonary function studies shown below.

Her 18th and last admission, [redacted]-63, was precipitated by the fact that her dyspnea, which was progressively increasing in severity, had become intractable and intolerable. She developed profound respiratory insufficiency, [redacted], persisted with high fever and even though her respiratory function was responding to therapy, she developed peripheral vascular collapse and died, [redacted].

She had developed a hypokalemic alkalosis, azotemia and respiratory alkalosis. Pathologic studies revealed she had a confluent Gram-negative bronchopneumonia with severe bronchitis and bronchiolitis as well as a severe hypoxic glomerulitis.

LAB DATA

	[redacted]	[redacted]	[redacted]	[redacted]
Hb	10	11	9.9	10.8
Hmct	35	43	35	35
WBC	9500	18,600	15,000	12,700
Diff	N	Left	Left	Left
BUN	10	25	90	---
CO_2 mM/L	30	40	24	27
Cl	95	88	88	86
Na	142	132	132	129
K	4.1	6.0	4.7	3.1
Urine, ml/24 hr.	---	300	75	400
Wt	47	---	48	46
pH	---	7.0	7.3	7.6
$PaCO_2$ mmHg	---	160	50	29
PaO_2 (100% O_2)	---	340	485	500
SaO_2% (Room Air)	---	65	---	---

PULMONARY FUNCTION DATA

	PRED.	1960	1962*	[redacted] 1963	[redacted]. 1963	[redacted]. 1963
Total Lung Cap. (ml)	4.94				6.48	
Residual Vol. (ml)	1.24				4.85	
RV/TLC (%)	25				75	
Forced Vital Cap. L	3.7	2.0	3.2	2.0	1.64	0.8
Forced Exp. Vol. 0.5 sec.	2.2	1.4	1.6-50%	0.49-25%	0.25	
Forced Exp. Vol. 1.0 sec.	2.8	1.6	2.1-65%	0.76-38%	0.40	0.2
Forced Exp. Flow 0-25% L/sec.	6.3		4.8-(77%)	0.87-(14%)		
Forced Exp. Flow 25-75%	3.4		1.14-(34%)	0.21-(6.2%)		
Forced Exp. Flow 50-75%	2.6		0.76-(29%)	0.12-(4.6%)		
Forced Insp. Flow	4.8		3.90-(81%)	2.1-(43%)		
Vit. Cap. Exhal. Time, sec.	4.0		6.2	12.3		
Pulm. Cap. Blood Flow, L/min.	5.5				17.4	
Memb. Diff. Cap., ml/min. x mmHg	72				51	
Cap. Blood Vol., ml.	167				168	

Markedly increased capillary blood flow cause undetermined.
Slightly decreased diffusing capacity and normal capillary volume.

[redacted]63	ROOM AIR	100% O_2	R. A. EXERCISE
pH	7.40	7.37	7.37
$PaCO_2$ mmHg	35	39	39
PaO_2 mmHg	78	675	67
V_E L/min	12.33	---	20.18
Resp. Rate	20		25
V_{O_2} ml./min.	287		619
V_{CO_2} ml./min.	296		574

* Steroids and hospitalization

CASE: [redacted]

A 39 year old white male who had mild to moderate allergic rhinitis for several years prior to age 35 when he first developed a persistent cough productive of mucopurulent sputum several ounces per day. He saw numerous physicians and was given antibiotics and antihistamines. Sputum cultures repeatedly revealed Pseudomonas aeruginosa. Allergy studies failed to yield anything but sensitivity to house dust. Sinus X-rays and clinical examination revealed persistent sinusitis and polyposis. He was a heavy cigarette smoker for some 15 years. WBC varied, and periodically there was marked eosinophilia 8-22%. He was given Polymyxin on several occasions with little success.

Progressive severe respiratory insufficiency with weight loss led to his admission to Methodist Hospital 4-6-61. He was hyperpneic, severely dyspneic, slightly cyanotic. Blood pressure was 134/92. Severe inspiratory and expiratory wheezing was noted, but there was no evidence of pneumonia. X-rays revealed marked overdistension of the lungs but no bullous lesions and no consolidation. WBC was 14,000 with 22% eosinophiles. Sputum, which was very thick and purulent, revealed a heavy growth of Pseudomonas. Bronchoscopy and bronchography revealed severe bronchitis especially involving the RML especially. He failed to respond to antibiotics: Penicillin, Tetracycline, Streptomycin and Polymyxin B, along with a moderate bronchial hygiene aerosol therapy. His condition was deteriorating, and he was having severe wheezing and dyspnea.

At this point, [redacted]-61, an intensive therapy consisting of bronchodilator by IPPB at 30 cm H_2O q. 2 h. with continuous heated mist of Tergemist and 2% propylene glycol was started. Postural drainage with chest clapping was done during IPPB treatments in a knee chest position. Sat. Sol. KI, 15 gtt t.i.d. pc, Medrol, 16 mg q.i.d., and Aminophylline suppositories, 500 mg q. 6 h were started. All antibiotics were stopped.

Copious amounts of thick mucopurulent material and some solid bronchial plugs were produced over the ensuing weeks with progressive functional improvement. He was discharged on a similar but modified program on [redacted]-61.

He was not seen again by us until [redacted], 1963, when he reported he was asymptomatic by September, 1961, when he stopped steroids and shortly thereafter stopped the nebulization treatment. In [redacted], 1961, he had a relapse of productive cough and wheezing dyspnea as always preceded by purulent nasal infection. He was under the care of an ENT surgeon who had done several procedures to correct his nasal problem and an internist who was concerned with his general care especially his hypertension which had persisted. He had no evidence of renal disease. He would improve each time on steroids, nebulization and antibiotics. He was recovering from one such episodes when seen in [redacted], 1963. He again had Pseudomonas infection in the nasal and bronchial secretions.

He was once again advised in regard to his therapy program and has done very well with only rare wheezing dyspnea. However, later he again abandoned his bronchial hygiene program but continues on steroids orally and by aerosol and Peractin oral and remains clinically well.

	[redacted] 1961		[redacted] 1963		[redacted] 1964	
	PRED.	ABD.	BBD.	ABD.	BBD.	ABD.
FVC	4.85	3.87	5.3	5.3	5.0	5.2
$FEV_{0.5}$	>60%	1.01-28%	2.7-51%	2.8-52%	2.9-58%	3.2-62%
$FEV_{1.0}$	>75%	1.48-38%	3.8-72%	3.9-74%	3.8-76%	4.1-79%
$FEF_{0-25\%}$	8.3	1.7(20%)	5.9(72%)	6.6(80%)	9.7(115%)	10.5(128%)
$FEF_{25-75\%}$	4.5	0.4(9%)	2.7(59%)	2.9(65%)	2.8(60%)	3.8(85%)
FIF	6.3	4.2(67%)	5.3(84%)	5.6(89%)	6.0(96%)	6.7(106%)
TLC	<6.5	7.2(110%)	---	7.25		
RV/TLC	<25%	46%	---	27%		
7 Min N_2 Index	1.5%	3.2%	---	1.5%		

	ROOM AIR REST	100% O_2	EXERCISE - 100% O_2
SaO_2%	96	100	100
PaO_2 mmHg	85	633	621
pH	7.45	7.45	7.34
$PaCO_2$ mmHg	37	37	44
$CaCO_2$ mM/L	22	23	23
P_AO_2	110	663	656
A-a O_2 grad.	25*	30	35

* Evidence only of a mild defect in distribution of ventilation to blood flow.

CASE: [redacted]

A twelve year old white male admitted [redacted], 1963, with severe asthmatic bronchitis. He was the product of a normal pregnancy and delivery and was well until 17 months of age at which time when he was noted to be extremely irritable and failed to walk. Diagnosis of Vitamin D resistant rickets was made which was treated fairly successfully; it has required treatment intermittently since. About the same time he began to have asthmatic attacks which have persisted intermittently ever since. His asthma has never been severe enough to precipitate a hospitalization for acute respiratory distress. However, since he has been three years of age, he has intermittently received ACTH and adrenal steroids in order to maintain complete symptomatic control. His only therapy has been steroids and oral or injection bronchodilator therapy. There is a family history of rickets and asthma on the paternal side of the family. Examination revealed blood pressure of 100/70; pulse was 70; respirations were 34; height was 50.5 inches. He is a well-developed, symmetrical child with no evidence of secondary sexual development. Lungs reveal evidence of marked overdistension of the chest with increased AP diameter, scattered areas of diminished breath sounds as well as inspiratory and expiratory wheezing and scattered crackling rales. The abdomen revealed two previous herniorrhaphy scars but otherwise no abnormalities. The genitalia were quite immature with virtually no pubic hair. Testes were small and atrophic. Skin is smooth and clear, almost pale, delicate and infant-like.

Laboratory studies included 24 hour urine, calcium - 256, phosphorous - 110, 17-hydroxycorticoids - 4.9. The PBI was 6.3; BUN was 17; fasting blood sugar was 55; sodium was 143; potassium was 4.5; CO_2 was 26; chloride was 103; calcium was 9.9; phosphorous was 3.8; alkaline phosphatase was 6.0; albumin was 5.3; globulin was 2.1. X-rays indicated a bone age of six years in this twelve year old boy. There is no evidence of active rickets or osteomalacia. A sweat sodium chloride test was negative. Initial sputum culture revealed Neisseria catarrhalis and Streptococcus viridans, but after several days of treatment, the patient began to raise old mucoid and mucopurulent plugs which when cultured revealed Pseudomonas aeruginosa which was sensitive to polymyxin, kanomycin, colymycin. The pulmonary function test summary is shown on the following page. Therapy consisted of aerolone compound bronchodilator, 10 drops, with Tergemist solution, 30 drops, by intermittent positive pressure breathing at 25 cm. of water pressure. He was also given Aminophylline, 250 mgms., before each meal and at bedtime, and each bronchodilator treatment which was given every two hours was followed by continuous heated mist aerosol of one part Tergemist, three parts distilled water with Propylene Glycol q s to 2%. Librium, 5 mgms. was used as a sedative one to three times daily to help allay his anxiety, and occassionally Aminophylline suppositories were used at night. On admission his white blood count was 9,000 with a normal differential. After the institution of aerosol therapy with the appearance of large numbers mucoid plugs in his sputum, the white blood count rose to 12,000 with 36% eosinophils which was also accompanied by exacerbation in his asthmatic symptoms with the gradual clearing of his sputum to the point where he was only raising clear mucous, and the asthmatic symptoms subsided, and the white blood count fell again to 5,000 with 6% eosinophils. Saturated solution potassium iodide, 7 drops, 3 times daily after meals was added to his therapy. He was not given any steroids, and after several days of vigorous bronchial hygiene, with clearing of the sputum, the Pseudomonas

disappeared from the sputum cultures. No antibiotic therapy had been given, but had the Pseudomonas persisted in the sputum, polymyxin or Colistyn aerosol with pancreatic Dornase would have been started by aerosol.

[redacted] 12 YR. W.M. 50 1/2 IN. 70 LBS.

	PRED.	ADM.	DAY 2	DAY 5	DAY 10 BBD	DAY 10 ABD
FVC	2.15	0.55 (26%)	1.2 (56%)	2.17 (100%)	2.33	2.54 (>100%)
$FEV_{0.5}$	>60%	0.23 42%	0.5 42%	0.85 40%	1.07	1.18 47%
$FEV_{1.0}$	>75%	0.33 60%	0.9 75%	1.23 57%	1.37	1.57 62%
$FEF_{0-25\%}$	3.6	0.75 (20%)	1.7 (47%)	2.24 (63%)	2.68	3.5 (96%)
$FEF_{25-75\%}$	2.0	0.27 (14%)	0.37 (19%)	0.56 (28%)	0.60	1.0 (50%)
FIF	2.8	0.74 (27%)	2.6 (90%)	2.82 (100%)	3.80	4.7 (>100%)

[redacted] 64 YR. RETIRED CABINET WORKER 4 HOSPITALIZATIONS FOR SEVERE RESPIRATORY INSUFFICIENCY WITH HYPERCAPNIA AND TWO EPISODES OF RT HT FAILURE PRIOR TO 1956.

	PRED.	1953 [redacted]	1953 [redacted]	1954 BBD	1954 ABD	1964 BBD	1964 ABD	1959 LOWEST MEASURED FUNCTION
FVC	3.6	1.8	3.7	3.8	4.0	4.1	4.6	1.5
$FEV_{0.5}$	2.15	0.5	0.9	0.9	1.1	0.9	1.2	0.3
$FEV_{1.0}$	2.70	0.8	1.5	1.5	1.6	1.4	1.9	0.5
$FEF_{0-25\%}$	6.1	1.1	1.5	1.6	2.3	1.9	2.5	0.6
$FEF_{25-75\%}$	3.4	0.4	0.5	0.5	0.6	0.5	0.5	0.4
FIF	4.7	2.5	3.6	3.5	4.0	3.0	6.0	2.0

REFERENCES

GENERAL REPORTS AND SYMPOSIA

1. American Thoracic Society: Definitions and classifications of chronic bronchitis, asthma, and pulmonary emphysema. A Committee Statement. Amer Rev Resp Dis 85:762, 1962.

2. CIBA guest symposium: A report, terminology, definitions and classification of chronic, pulmonary emphysema and related conditions. Thorax 14:286, 1959.

These statements essentially agree although the former is somewhat more comprehensive.

3. Orie, N.G.M., and Sluiter, H. J.: Bronchitis. An International Symposium. University of Gronigen, The Netherlands. Royal Van Gorcum, publishers, 1961.

4. New York Academy of Science: A symposium on mucous secretions. Part VI: Studies on mucous in relation to human disease. Part V: Factors affecting mucous and its secretion. Annals of the New York Academy of Science, 103:583-756, March, 1963.

5. Surgeon General's Report on Smoking and Health: Section on chronic bronchitis and emphysema. Publication # 1103:278-313, including 194 references. Published by the U. S. Dept. of Health, Education and Welfare. U. S. Government Printing Office, 1964.

6. Reid, D. D., and Fairbairn, A. S.: The natural history of chronic bronchitis. Lancet 1147, May 31, 1958.

This is a study in a stable population of postal workers that those who ultimately became disabled or died prematurely of chronic bronchitis had more and longer absences from work even in early adult life due to respiratory diseases. This same group had 8 to 10 times as many attacks of pneumonia or acute bronchitis as their controls. Illness associated with respiratory attacks was more prolonged in the bronchitic as compared to the controls. This was definitely related to fog and coldness.

7. Medvei, V. C., and Oswald, N. C.: Chronic bronchitis: a five year follow-up. Thorax 17:1, March 1962

This and the Reid study indicate a five fold increase in mortality rate in bronchitics.

8. Fletcher, C.M.: An account of chronic bronchitis in Great Britain with a comparison between British and American experience of the disease. Dis Chest 44:1, July 1963.

ETIOLOGICAL CONSIDERATIONS

9. Auerbach, O., Stout, A. P., Hammond, E. C., and Garfinkel, L.: Changes in bronchial epithelium in relation to sex, age, residence, smoking and pneumonia. New Eng J Med 267:111, 1962.

10. Auerbach, O., Stout, A. P., Hammond, E. C., and Garfinkel, L.: Bronchial epithelium in former smokers. New Eng J Med 267:119, 1962.

11. Auerbach, O., Stout, A. P., Hammond, E. C., and Garfinkel, L.: Smoking habits and age in relation to pulmonary changes. New Eng J Med 269:1045, 1963.

These exhaustive studies performed in a double-blind fashion with matching controls conclusively reveal the extensive bronchoalveolar changes caused by cigarette smoking and the regression of these signs with the withdrawal of cigarette smoking. The findings emphasized hyperplasia and metaplasia of the bronchial epithelium, atypically nucleated cells, gland hyperplasia and increased numbers of goblet cells, rupture of alveolar septums, fibrosis and thickening of the walls of small arteries.

12. Murray: Chronic bronchitis in England. J Chronic Dis 15:991, 1962.

13. Dates, D. V., et al: Chronic bronchitis in Canada. Med Serv J Canada 18:211, 1962.

Both of these articles again point up cigarette smoking and atmospheric polution as the principal etiologic factors related to chronic bronchitis. Ventilatory impairment with normal diffusing capacity is the principal functional manifestation.

14. Fletcher, C. M., Hugh-Jones, P., McNicol, M. W., and Pride, N. B.: Diagnosis of pulmonary emphysema in presence of chronic bronchitis. Quart J Med 33:33, 1963.

This extensive and meticulous study demonstrates that the terms chronic bronchitis and emphysema are not synonymous. Moreover, conditions are not necessarily pathogenetically related. Severe bronchitis does not necessarily result in an important degree of emphysema. It is apparent that careful, clinical, radiological and functional examination will help to differentiate these disturbances.

15. Hentell, W., Longfield, A. N., Vincent, T. N., Filly, G. F., and Mitchell, R. S.: Fatal chronic bronchitis. Amer Rev Resp Dis 87:216, 1963.

This is a detailed, clinical, physiological and morphological study of four cases of severe, chronic bronchitis demonstrating that bronchitis can be fatal with major emphysema.

16. Simpson, P., Heard, B., and Laws, J. W.: Severe irreversible airways obstruction without emphysema. Thorax 18:361, 1963.

17. Gandevia, B. and Cowling, D. C.: Bacteriological studies in chronic bronchitis. Aust Ann Med 10:275, 1961.

This report emphasizes the fact that while H influenza and D pneumoniae are recognized as the principle pathogens in chronic bronchitis (and now in addition probably viruses). Other bacteria ordinarily suppressed by antibiotics should be considered very important in the progression of chronic bronchitis. These include Gram-negative infections such as E coli, Pseudomonas klebsiella and also Staph pyogenes as well as proteus. These authors emphasize the possibility that organisms ordinarily considered non-pathogenic may be pathogenic for the bronchitis.

18. May, R. J.: Pathogenic bacteria in chronic bronchitis. Lancet, P. 839, Oct. 23, 1954.

In addition to again emphasizing the importance of H influenza, and D pneumoniae these authors emphasized the importance of culturing purulent sputum because of the purulent nature of eosinophilic sputum which may not be infected.

19. Fry, J.: Fate of 424 patients with pneumonia and bronchitis. Brit Med J 5211:1483, Nov. 19, 1960.

This author found that among chronic bronchitics, male smokers of lower social classes developed disability with bronchitis most rapidly. Overall, 71% of the patients diagnosed as having bronchitis were disabled after ten years from the time of the initial diagnosis.

20. Corelli, A. D., Dohd, R. S., and Gordon, W.: A virological study of chronic bronchitis. New Eng J Med 270:123, 1964.

These and other studies cited indicate that viral and other non-bacterial agents may be the most important cause of acute respiratory exacerbations experienced by patients with chronic bronchitis.

21. Muir, D., Batten, A., and Simon, G.: Mucoviscidosis and adult chronic bronchitis: their possible relationship. Lancet 1:181, 1962.

22. Polgar, George, and Denton, R.: Cystic fibrosis in adults: studies of pulmonary function and some physical properties of bronchial mucous. Amer Rev Resp Dis 85:319, 1962.

It has been considered possible that there may be some etiological relationship between the hypersecretory state of chronic bronchitis and that of mucoviscidosis or cystic fibrosis. The possibility still remains that some cases of chronic bronchitis are variants of cystic fibrosis. All of the supporting evidence such as the finding of other manifestations of cystic fibrosis (increased sweat sodium chloride or abnormal pancreatic enzyme function) are generally lacking.

23. Seebohm, P. M., and Bedell, G. N.: Primary, pulmonary emphysema in young adults. Amer Rev Resp Dis 87:41, 1963.

This study serves only as a supplement to the Fletcher study in that it emphasizes the fact that emphysema can occur without significant

bronchits. Virtually all of the so called primary, pulmonary emphysema patients reported in this and other series were heavy cigarette smokers. It is very likely that the lesion in these cases is degenerative parenchymal damage resulting from a bronchial or alveolitis such as reported by Anderson et al, Diseases of the Chest, Vol. 43, page 350, 1963.

24. Kurung, Joseph M : Examination of sputum. Amer Rev Resp Dis 76:671, 1957.

Proper collection of a sputum specimen is emphasized including proper instruction of the patient to get his cooperation in obtaining a specimen from the lungs, careful brushing of the teeth and cleaning of the mouth before expectoration of the specimen and collection of the early morning sputum. Technique: place a fleck of sputum on a slide; add a drop or two of 10% sodium hydroxide; cover with a cover slip. Elastic tissue fibers will be seen as distinct, slender, wavy, highly refractile fibriles, uniform in diameter but variable in length usually with spread or frayed ends since elastic fibers are distributed in the walls of alveoli, and the bronchi and blood vessels are present since sputum indicates an active destructive process.

25. May, J.R., and May, D.S.: Bacteriology of sputum and chronic bronchitis. Tubercle 44:162, 1963.

These British authors again find hemophilus influenza as the most important pathogen in the sputum of patients with chronic bronchitis. It was found significantly more frequently in specimens containing pus than in those containing no pus. Sputum culture was carried out after preliminary liquifaction by pancreatin because without pancreatin, isolation rate of hemophilus influenza was only 50% of that with pancreatin. No alteration or sensitivity organism to penicillin or tetracycline was found after more than five months of therapy with these drugs.

26. Miller, D.L.: A study of techniques for the examination of a sputum in a field survey of chronic bronchitis. Amer Rev Resp Dis 88:473, 1963.

27. Chodosh, S., Zaccheo, C. W., and Segal, M.: Cytology and histochemistry of sputum cells. Amer Rev Resp Dis 85:635, 1962.

28. Pecora, D. V.: A comparison of transtracheal aspiration with other methods of determining bacterial flora of the lower respiratory tract. New Eng J Med 269:664, 1963.

This was demonstrated to be the most reliable method for obtaining culture material from the lower respiratory tract. Studies failed to reveal that the majority of patients with symptoms generally attributed to "chronic bronchitis" harbor bacteria in the lower respiratory tract.

29. Glynn, A. A., and Michaels, L.: Bronchial biopsy in chronic bronchitis and asthma. Thorax 15:142, 1960.

Results in 45 patients with chronic bronchitis or asthma. Asthmatics differ in that they consistently revealed a heavy infiltration of eosinophils in the lamina propia.

30. Cole, Milton B., et al: Longitudinal studies in emphysema; III sputum eosinophilia. Amer Rev Resp Dis 80:915, 1959.

Periodic "in Sauers" of sputum eosinophilia unrelated to gross sputum characteristics, patient's symptoms or meterological conditions were found frequently in spite of the absence of any evidence of allergy. Findings also unrelated to sputum flora. No data on blood eosinophilia.

31. Erlich, H.: Bacteriological studies and effects of anesthetic solutions on bronchial secretions during bronchoscopy. Amer Rev Resp Dis 84:414, 1961.

This study indicates a variable inhibition of bacterial growth including M tuberculosis from sputum specimens obtained after topical anesthesia for bronchoscopy. Variability and inhibition was felt to be related to duration and amount of exposure to anesthetic agent as well as viscosity of sputum which is increased tended to protect organisms against the effects of the anesthetic agent.

PATHOLOGY

32. Reid, Lynne: Pathology of chronic bronchitis. Lancet 1:275, 1954.

This was the first real description of the changes associated with this disorder in relationship to the stages of severity of the disease. The following early changes were described: hypertrophy of goblet cells, purulent bronchiolitis, small peribronchial abscess cavities, obliteration of the lumen in some instances, and ultimately either localized or diffuse dilatation of the peripheral bronchi. In more advanced stages alveolar changes appear along with an organizing pneumonia, areas of collapse with mucous plugging.

33. Reid, Lynne: Measurement of the bronchial mucous gland layer. A diagnostic yardstick in chronic bronchitis. Thorax 15:132, 1960.

The method involves comparing thickness of the bronchial wall with thickness of the mucous gland at the same point, thus establishing gland to wall ratio which was of significant value in differentiating patients with bronchitis from those with emphysema.

34. Thurlbeck, W. N.: A clinical, pathological study of emphysema in American hospitals. Thorax 18:59, 1963.

This report is of significance in that all cases of severe emphysema, a history of chronic bronchitis was present in 85% while in the remaining 15%, hypertrophy of the bronchial mucous glands were present even though a clinical history of chronic bronchitis had not been recorded. The significant etiological factors in order of relative importance were smoking, pulmonary infections other than bronchitis and asthma. There was also a direct correlation between the severity of the emphysema and the severity of cigarette smoking.

35. Papanicolaou, G. N., Bridges, E. L., and Railey, C.: Degeneration of ciliated cells of bronchial epithelium (cilio, cyto, phthoria) in its relation to pulmonary disease. Amer Rev Resp Dis 83:641, 1961.

This is a detailed discussion of the degenerative changes of the ciliated columnar epithelium of the bronchial tree. Changes were divided into three main groups, one - alteration of the nucleus characterized by pyknotic, deep staining disruption of nuclear pattern and chromatin clumping; two - cytoplasmic alterations, acidophilic inclusion bodies, deprivation of cilia; the inclusion bodies may be particles of altered chromatin similar to that found in severe viral infections; three - changes denoting disintegration of the cell including fragmentation, division, loss of nucleus or complete disintegration into an amorphus mass.

36. Thurlbeck, W. N., and Angus, G. E.: The relationship between emphysema and chronic bronchitis as assessed morphologically. Amer Rev Resp Dis 87:815, 1963.

37. Hirschfeld, J. H.: Dilated bronchial mucous glands in chronic bronchitis: a neglected morphologic finding. Correlation of bronchoscopic and bronchographic appearance. Amer Rev Resp Dis 83:16, 1961.

38. Olivia, V. S., Bradley, C. G., and Williams, S. F.: Pathognomonic signs of chronic bronchitis. Amer J Roentgen 83:274, 1960.

This study emphasizes active inspiratory, expiratory bronchography and the findings of bronchial gland dilatation, bronchiolar diverticulosis, distortion of bronchial walls with abnormal changes in caliber on inspiration, expiration and varying degrees of coincident emphysema and fibrosis.

39. Gandi, and Sannazzari, T. L.: Radiological investigations in bronchorrea: I. Chronic bronchitis. Radiol Med (Torino) 45:420, 1959.

Stratibronchography was very valuable in defining the parenchymal as well as the bronchial lesions while angiopneumography provides a direct view of the pulmonary vessels. The principal bronchographic features are diverticuli of the mean bronchi, ectasia of the peripheral bronchioli, irregular caliber of the dividing bronchi, variability in the thickness of the bronchial walls from atrophy to hypertrophy.

40. Dunnill, M. S.: The pathology of asthma with special reference to changes in the bronchial mucosa. J Clin Path 13:27, 1960.

On gross section, the lungs showed the presence of mucous plugs throughout the respiratory passages causing focal areas of collapse. Histologically, the prominent features are marked mucosal edema, disruption and shedding of the columnar epithelium with loss of cilia, mucosal metaplasia with cuboidal and stratified epithelium, thickening

of the basement membrane and frequently eosinophilic infiltration. The author concludes bronchospasm appears to play little or no role in the pathogenesis of an asthmatic attack.

41. Johnson, R. S., and Sita-Lumsden, E. G.: Plastic bronchitis. Thorax 15:325, 1960.

British term for the condition known as mucoid impaction in this country. That is one of the important complications of eosinophilic bronchitis. This condition may mimic tumor, tuberculosis or other disorders.

PHYSIOLOGY

42. McNab, G. R., Grove, W. S., and Nariman, S.: A comparison of physiological and pathological findings in chronic bronchitis and emphysema: response to exercise. Thorax 16:56, 1961.

43. Ting, E. Y., and Williams, M. H., Jr.: Mechanics of breathing in chronic obstructive pulmonary disease. Amer Rev Resp Dis 88:791, 1963.

44. Williams, M. H., Jr., and Seriff, N. S.: Chronic obstructive pulmonary disease: An analysis of the clinical, radiological and physiological features. Amer J Med 35:20, 1963.

45. Wells, R. E., Jr.: Mechanics of respiration in bronchial asthma. Amer J Med 26:384, 1959.

TREATMENT - ANTIBIOTICS

46. Francis, R. S., May, J. R., and Spicer, C. C.: Chemotherapy of bronchitis. Report to the research committee of the British Tuberculosis Association. Brit Med J 5258:979, 1961.

47. Gandevia, B., and Cowling, D. C.: Antibiotic therapy in chronic bronchitis. Med J Aust, Nov. 18, 1961, recommend initial control of purulent infection in the bronchitic be accomplished with 4 to 6 million units of penicillin and two grams of streptomycin daily or tetracycline, 3 grams daily, either method for five to seven days. Tetracycline is then continued one gram daily with increases to two grams in the presence of exacerbation. They emphasize that any attempt at long term control should be dealt with by initial complete clearing of the patient's sputum.

48. Norman, P. S.: Antibiotics in chronic bronchitis and bronchiectasis. J Chronic Dis 15:719, 1962. JAMA 179:833, March 17, 1962.

This and other studies which show distinct benefit in terms of control of daily symptoms, reduction in the incidence of exacerbation and reduction in the number of positive cultures for for hemophilus and pneumococcus in patients with chronic infective, bronchial disease again raises the interesting questions as to why tetracycline has

such peculiar clinical efficiency not shared by other antibiotics. Whether regular use of these agents will alter the ultimate course of the disease is still unknown. Tetracycline is known to be effective against three agents that have been linked with bronchitis, hemophilus influenza, pneumococcus and Eaton agent.

49. Dowling, H. F., Leper, Mark H., and Jackson, G.G.: Commentary suppresive therapy of chronic bronchial infection. Clin Pharmacol Ther 3:564, 1962.

This is the best summary of all work done to date which leads to the conclusion that continuous tetracycline therapy is the most effective method of antibiotic administration devised for diminishing the frequency of exacerbation in patients with chronic bronchial infection. I would point out that there are no studies with comparison of comparable subjects utilizing effective bronchial hygiene measures. In this review, it was reported that some patients had taken continuous tetracycline therapy for periods up to five years with no untoward side effects.

50. Edwards, G., Charley, D. J., Keal, E. E., and Fear, E. C.: Treatment of acute bronchitic exacerbation. Thorax 18:90, 1963.

51. Tyler, L. E.: Treatment of exacerbations of chronic bronchitis ampicillin. Brit J Clin Pract 17:321, 1963.

This bacteriacidal agent is reported to be effective against H influenzi and pneumococcus without significant side effects.

52. Millard, F. J. C., and Batten, J. C.: Comparison of ampicillin and tetracycline in chronic bronchitis. Brit Med J 5331:644, 1963.

Continuous therapy was utilized in 52 patients alternating 500 mgms. b.i.d. of these drugs. No significant difference was found except for somewhat greater reduction in the quantity of sputum noted with ampicillin.

53. Louya, D. B., and Kaminski, T.: Effects of four antimicrobial drug regimens on sputum superinfection in hospitalized patients. Amer Rev Resp Dis 85:649, 1962.

The use of large dose, multiple, antimicrobials in hospitalized patients with pulmonary infections is potentially a considerable danger to the patient because of superinfection. The most desirable regimen consists of the smallest amount of the appropriate drug necessary to suppress effectively or eradicate the invading organisms. These studies further tend to suggest the safety of single drugs, prophylactic therapy.

54. Leper, Mark H.: Opportunistic Gram-negative rod pulmonary infection. Dis Chest 44:18, 1963.

Opportunistic infections of the lungs more often develop in hospitalized patients who have some form of underlying disease and constitutes a distinct threat in patients with pre-existing chronic bronchitis. In this study 38% developed staphlococcal infections, 35% Gram-negative rod infections, and 27% mixed staphlococcal and ram negative rod infections.

An overall incidence of hospital acquired pneumonia, 20% was observed for this group of patients.

55. Yow, E. M.: Development of proteus and pseudomonas infections during antibiotic therapy. JAMA 149:1184, 1952.

TREATMENT - OTHER AGENTS

56. Webb, Watts R.: Clinical evaluation of a new mucolytic agent, acetylcysteine. J Thorac Cardiov Surg 44:330, 1962.

N-acetylcysteine is a derivative of amino acid, acid-cysteine which is effective in liquefying mucous and desoxyribonucleic acid, but has no effect on fibrin or blood clots. Mucolysis is accomplished by clevage of disulphide bonds, by the sulfhydryl groups of this agent. It apparently does not attack living tissue in that unlike proteolytic enzymes, it does not disrupt peptid linkages in proteins. (This agent has been used extensively in this hospital system and is most effective by direct instillation techniques, either through transtracheal catheters or endobronchial plastic catheters. It can also be administered by aerosol. This substance reacts with rubber and metal and therefore, these materials must be avoided. It is a potent physical irritant; therefore, its usefulness must be carefully evaluated in those instances where there is some doubt about the need for bronchial lavage. One must always be prepared to evacuate the material that is mobilized if the patient's efforts are inadequate or ineffective. WFM)

57. Palmer, K. N. V., Geake, M. R., and Brass, W.: Clinical trial of methylcysteine hydrochloride in chronic bronchitis. Brit Med J 1:280, 1962. (an oral mucolytic agent)

58. Bruce, R. A., and Quinton, K. C.: Effective oral alpha chymotrypsin or sputum viscosity. Brit Med J 1:282, 1962.

59. Palmer, K. N. V.: New mucolytic agent by aerosol (Ascoxal) for inhalation in chronic bronchitis. Lancet 2:802, 1961.

This is a peroxide combination not available in this country.

60. Plestin, M., and Stuart-Harris, C. H.: Steroid therapy in chronic bronchitis. Lancet 1:1311, 1962.

This was a short term therapy study showing 65% of the patients to improve, both functionally and symptomatically. The authors felt that the role of steroids in the treatment of chronic bronchitis was held somewhat in doubt as the result of this short term study and pointed out the increased danger of bacterial pneumonia. No comment was made on the relationship between steroid therapy, antibiotic therapy and other symptomatic measures.